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Prevalence of Asthma and Related Symptoms in Primary School Children of Isfahan, Iran, in 1998

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SUMMARY **As developing countries adopt an industrialized style of living, an increase in asthma prevalence can be expected. A cross sectional study was undertaken to evaluate the prevalence rates of asthma and related symptoms and clinical findings in Isfahan, Iran. A randomly selected population of Isfahan primary school children, consisting of 3,982 children aged 6 to 11 was enrolled in the study. Parents completed a Persian questionnaire modified from ISAAC and ECRHS questionnaires. The returned 3,828 (96.1%) questionnaires were reviewed and 686 children suffering from asthma or any of the related symptoms were invited for further evaluations. In this stage 655 children (95.5%) underwent a medical interview and physical examinations, of which 415, underwent post exercise spirometry and body-plethysmography. The prevalence rates for previously diagnosed asthma, dyspnea and wheezing ever, dyspnea and wheezing in the last 12 months and frequently recurring dyspneal attacks were 0.71%, 7.6%, 3.9% and 1.6%, respectively. Wheezing was heard upon auscultation of the chests of 70 children (10.7%). Forced expiratory volume in 1st second (FEV1) < 80% of prediction was recorded in 3.1% of the children, other findings included reduced peak expiratory flow rate (PEF), mean expiratory flow 25 to 75 percent (FEF 25-75), forced expiratory flow at 75% of FVC (FEF 75), and increased residual volume (RV) and air-ways resistance in 4.3%, 10.6%, 21.2%, 30.1% and 63.2% of the pupils, respectively. We conclude that asthma screening programs employing clinical methods should be encouraged, but measurement of airway resistance is not a suitable tool for epidemiologic studies.**

There is great concern over the worldwide increase in prevalence of asthma[1-7] especially in children.[8-12] However, the true extent of the problem is not well clarified.[13,14] Data reported from developed countries show higher prevalence rates than those from developing countries[15,16] and Southeast Asia.[14] Scattered epidemiologic studies from the Middle East have just recently been started to be published.[17-20]

Epidemiologic studies based on ISAAC protocols have contributed enormously valuable information concerning the prevalence of asthma and it's geographic variability. However, verification of the epidemiologic findings by clinical methods including medical interview, physical examinations and physiologic measurements can enhance the accuracy of the results of epidemiologic studies.

Isfahan is an ancient city with a temperate dry climate, situated in the western margin of the central deserts of Iran. The city had originally been founded for commercial purposes, but during the last 50 years many industries have been established in Isfahan and the face of the city has changed to an industrial city. There is almost always a relatively high level of combustion related air pollution, so that many of the ancient beautiful sights of the city are usually hidden by the thick polluted air. This heavy air pollution can cause increased prevalence of respiratory disorders including asthma. The total popula-

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tion of Isfahan urban area is approximately 1.6 million people. In most days of the year, barometric pressure of the city is 84.4 kp (630 mm Hg). The purpose of this study is to determine the prevalence of asthma in the urban areas of Isfahan by clinical methods.

MATERIALS AND METHODS

A cross-sectional study was carried out in 1998 on a randomized sample of 3,982 schoolchildren. The review board for medical ethics, of the Isfahan medical school approved the study and methods. Assuming an asthma prevalence rate of 3-5% in the community, a sample of 1,824 pupils was originally estimated to be satisfactory for the purpose. Since the cases had to be selected by proportional random cluster sampling, the sample size was doubled and 3,648 pupils were decided to be enrolled in the study. These 3,648 children were expected to be in 101 school classes. In the study period in 1998 there were 5,300 primary school classes in the Isfahan urban area attended by 191,023 children, out of which 101 classes were randomly selected. The sample composed of all children attending the selected classes. Since some of the selected classes had more than the expected number of pupils, the final number of our subjects reached to 3,982 cases. The expected age of the population was from 6 to 11 years.

We developed a Persian questionnaire modified from pre-existing questionnairs.[7] The questions contained all of the respiratory questions of the International Study of Asthma and Allergies in Childhood (ISAAC).[7] We supplemented the questionnaires with additional questions concerning the parents' education and smoking habits, family history of asthma, housing conditions, pets and/or insects in the household.

A two step approach was used for the survey. In the first step, five interns of the Isfahan medical school attended the selected classes repeatedly to make friendly relationships with the students and urge them to cooperate. They met all of the pupils, explained the questions to them and mimicked the wheezy breathing for all of them to ensure that they have all understood the meaning of the questions. At this point the questionnaires were given to the students to be completed at home with their parents' assistance. Many times repeated visits at the schools were necessary to find children who had been absent in previous occasions. Also those students who did not return the questionnaires in due time, were visited at home to see the parents to seek more cooperation.

In the second step of the survey, we carefully reviewed the returned questionnaires, and 686 children who had admitted to have a previous diagnosis of asthma or any of the asthma related symptoms were referred to the pulmonary clinic of St. Zahra Medical Center of the Isfahan Medical School to undergo a medical interview, physical examinations, and a post exercise spirometry followed by body-plethysmography. After completion of exercise and a few minutes of resting, the chest was auscultated again. Medical interview and physical examinations were conducted by residents of medicine and supervised by the pulmonologist co-author. The abnormal findings were recorded. Only wheezy sounds at chest auscultation were interpreted as an asthma finding and presented here.

The subject's height was measured in stocking feet against a wall with a right angle. Spirometric measurements were performed using an electronic spirometer and body-box (Master-lab-Body Erich-Jaeger, Wurzburg, Germany) which was calibrated each morning, using a two-liter calibration syringe. After eight minutes of fast jogging, and five minutes rest subjects started spirometric measurements, carried out several forced vital capacity maneuvers, to obtain three consistent flow-volume loops, with FEV1 and FVCs close to each other to meet published standards.[22] Then body plethysmographies were performed and, total lung capacity (TLC), residual volume (RV), and airway's resistance were calculated.

Endo-bronchial provocation tests were not used because many of the parents were concerned about safety of the inhalation provocative agents and refused their use.

All spirometries were performed in a sitting position with a nose clips on the nose. We recorded: heights in centimeters (cm), volumes in liters (l), flows in liter/second (l/s) and resistance as kp/l/s (1 kp = 10.2 cm H_2O).

Eleven spirometric and 16 body-plethysmography recordings did not meet the standard criteria and were discarded.

Two hundred and thirty children (33.5%) who failed to come to the clinic after several invitations, were interviewed at school, but spirometry was not

done in this situation. One child with bronchiectasis and thoraco-abdominal situs inversus assumed to have Kartageners syndrome, was excluded from the series in order to be able to attribute all of the obstructive pulmonary function findings to asthma. Twenty-nine eligible students did not participate in any of the stage two surveys for unknown reasons and were excluded from the study.

We completed all of the step two evaluations, during a four months period from February to May 1998. The data obtained from the questionnaires, interviews and pulmonary function studies were collected in a database and analyzed by the statistical package for the social sciences (SPSS for Windows version 9.05). Logistic regression analysis was used for evaluation of the correlation between the asthma-related symptoms and possible risk factors.

In this study diagnosed asthma is any history of asthma previously diagnosed by a physician. Asthma-ever is defined as any history of wheezy breathing associated with dyspnea. Current asthma is defined as a history of at least one attack of wheezy breathing and dyspnea during the last 12 months, and persistent asthma is defined as frequently disturbing asthmatic attacks resulting in absence from school with more than 4 such attacks during the last 12 months. Exercise induced asthma is defined as occurrence of dyspnea and wheezing during or shortly after completion of jogging in the hospital garden. We also defined asthma-related symptoms to be: history of wheeze, dyspneal attacks associated with wheezy breathing, chronic intermittent dyspnea and/or cough, exercise induced cough and/or wheeze, frequent sleep disturbances at night due to coughs or chest illness. All of the mentioned conditions had to be confirmed in medical interview.

The cumulative prevalence rates for diagnosed asthma, respiratory allergies, wheeze, and wheeze associated with shortness of breath are based on symptoms since birth. All other symptom categories refer to symptoms within 12 months preceding the receipt of the questionnaires.

RESULTS

A total of 3,858 completed questionnaires were collected from the 3,982 pupils originally selected for the survey (96.9%) from which 30 cases who did not participate in second stage of the study were excluded. The male to female ratio was 1.04 (1,966 boys *vs* 1,892 girls). This pattern of sex distribution exactly reflects the sex distribution of the whole student population of Isfahan during the study period (Table 1). Finally 426 of the 686 symptomatic children (62.1%) attended the clinic for pulmonary evaluation, and 230 were interviewed at the schools. The prevalence of individual symptoms by sex is displayed in Table 2. The overall prevalence rates for asthma ever, current asthma, persistent asthma, exercise induced asthma, and chronic cough were 7.6%, 3.9%, 1.6%, 1.8% and 11.2%, respectively.

In our series the label "asthma" has been given 1.4 times more frequently in boys than in girls. Also all of the mentioned asthma-related symptoms including: wheeze, wheeze and dyspnea, night chest illness and abnormal lung sounds were more prevalent in boys than in girls in the early age, but gradually the difference diminished with advancing age. All of the described asthma related symptoms, either cumulative or currently active, showed an steadily increasing trend with increasing age of the population; however, an exceptional spike in frequency of symptoms was noticed in the seven years old girls.

Large family sizes were obviously common among the population, number of siblings ranged from 0 to 9, and many of the responders reported to have two to nine siblings with a mean of 2.9.

Nearly 50% of fathers (1,860 individuals) and 46% of mothers (1,735 individuals) had high-school education, while only 518 fathers (13.6%) and 227 mothers (6%) were university graduates. Nine hundred and ninety-one fathers (25.9%) and only 59 mothers (1.5%) were current smokers. Nearly all of the 3,828 participants reported to have carpets in their sitting rooms and most also had carpets in the bedrooms, therefore, it could not be classified as a risk factor.

Logistic regression analysis to evaluate possible relationships between symptom categories and risk factors was performed, at which no statistically significant relationship was found between the ailments and parental smoking habits, parental education or family size.

History of asthma in parents and/or siblings was strongly correlated with asthma in the children ($p < 0.001$).

Cockroaches had been visible in the living rooms and kitchens

Table 1 Population database

	Male (%)	Female (%)	Total (%)
Total population of Isfahan school-children aged 6-12 years	99,000 (51.8%)	92,000 (48.2%)	191,000 (100%)
Stage I			
Target population	2,028 (51%)	1,954 (49%)	3,982 (100%)
Responders	1,951 (51%)	1,877 (49%)	3,828 (100%)
Stage II			
Target population	349 (50.8%)	337 (49.2%)	686 (100%)
Responders			
Medical interview	331 (95.4%)	324 (96.1%)	655 (95.7%)
Physical examinations	331 (95.4%)	324 (96.1%)	655 (95.7%)
Post exercise spirometry	331 (95.4%)	324 (96.1%)	655 (95.7%)
Post exercise body-plethysmography	245 (70.5%)	170 (49.6%)	415 (60.5%)

Table 2 Respiratory symptoms according to questions, interview and physical examinations

Questions and/or clinical findings	Male 1,951 (100%)	Female 1,877 (100%)	Total 3,828 (100%)
1. Have you frequently had pulmonary infections diagnosed by a physician (2 times or more per year)?	50 (2.6%)	31 (1.7%)	81 (2.1%)
2. Do your colds usually go to chest?	789 (40.4%)	765 (40.8%)	1,554 (40.6%)
3. Did your coughs last for a month or more this year (last 12 months)?	106 (5.4%)	136 (7.2%)	242 (6.3%)
4. Have you ever had a respiratory allergy as told by a physician?	70 (3.6%)	46 (2.5%)	116 (3%)
5. Have you ever had wheezy breathing?	301 (15.4%)	282 (15%)	583 (15.2%)
6. Have you ever had wheezy breathing and dyspnea?	164 (8.4%)	129 (6.9%)	293 (7.6%)
7. Have you ever had asthma diagnosed by a doctor?	21 (1.1%)	6 (0.32%)	27 (0.71%)
8. Does running or playing football usually make you cough?	73 (3.7%)	128 (6.8%)	201 (5.2%)
9. Did you have wheezy breathing and dyspnea during the last 12 months?	71 (3.6%)	83 (4.4%)	154 (4%)
10. Did you wake up at night during the last 12 months due to an attack of chest tightness and/or cough?	170 (8.7%)	194 (10.3%)	364 (9.5%)
11. Frequent attacks(more than 4) of dyspnea and wheezy breathing in the last 12 months, resulting in school absence?	35 (1.8%)	28 (1.5%)	63 (1.6%)
*12. Presence of rhinitis, rhinorrhea and/or nose block on physical exam?	164 (49.2%)	80/24.7%	244/37.3%
*13. Presence of wheezing on chest auscultation.	41 (12.4%)	29/9%	70/10.7%

*Extracted from medical interviews and the percentages are calculated out of the 655 participants

in 1,736 instances (45.4%); the postulated asthmatics reported it more than the healthy children ($p < 0.04$).

The most popular pets kept by children in the series were chicken (12.8%), pigeons (8.2%), canaries (6.8%), and cats (5.7%). Dogs were uncommon pets in Isfahan households (0.5%), with a popularity not higher than lambs (Table 3). Among the reported pets, only the presence of birds was positively related to asthma and associated symptoms ($p < 0.02$).

Post exercise wheezing was heard over the chest of 70 children (10.7% of the step 2 population). The results of pulmonary function studies are shown in Table 4.

DISCUSSION

The absence of epidemiologic gold standard criteria for asthma diagnosis[12] makes symptom surveys effective tools.[7] The present survey is not an ISAAC study; however, we have used the core questions used in that kind of studies. Since we had intended to do medical interviews and physical examinations, the age groups suitable for ISAAC were not necessarily the best for our study and we decided to enroll primary school children of all ages to observe age related changes on the frequency of the condition.

To our knowledge, this is the first survey on the prevalence of parent reported physician diagnosed asthma and related symptoms in Iranian children. A relatively large randomly selected sample of 3,982 pupils was studied, and the response rate (96.2%) was excellent. Therefore, estimated prevalence rates can be considered as reliable. We could not obtain the parents permission to use histamine or methacoline for provocation,

Table 3 Pet keeping habits of Isfahan children

Pet	Frequency	%
Canary	262	6.8
Chicken	490	12.8
Pigeon	313	8.2
Cat	218	5.7
Dog	20	0.5
Lamb	17	0.5

Table 4 Pulmonary function tests results

Spirometric findings*	Male 245 (100%)	Female 170 (100%)	Total 415 (100%)
1. FVC < 80%	13 (5.3%)	18 (11%)	31 (7.7%)
2. FEV_1 < 80%	9 (3.7%)	4 (2.4%)	13 (3.1%)
3. FEV_1/FVC < 80%	15 (6%)	3 (1.8%)	18 (4.3%)
4. PEFR < 80%	43 (17.6%)	48 (28%)	91 (22%)
5. FEF25 < 70%	11 (4.5%)	11 (6.4%)	22 (5.2%)
6. FEF50 < 70%	27 (11%)	15 (8.8%)	42 (10.1%)
7. FEF75 < 70%	58 (24%)	30 (17.5%)	88 (21.2%)
8. FEF25-75 < 70%	31 (12.7%)	13 (7.6%)	44 (10.6%)
9. Residual volume > 110%†	52 (27.8%)	61 (32.3%)	113 (30.1%)
10. Airways resistance > 0.4 Kp (4 cm H_2O)/l/s†	146 (59.8%)	113 (68%)	259 (63.2%)

*All of the spirometric parameters have been calculated in percent of prediction except for FEV1/FVC which is expressed in percent of FVC and effective airway resistance which is in kp/l/second
† Cases with sub-optimal residual volume and/or resistance measurements have been excluded

which would have provided a more objective measure of asthma prevalence, instead we used exercise as a less potent but more acceptable provocation, which can partially compensate for this limitation.

Measurement of residual volume and airway resistance, which has not been used in previous epidemiologic studies at least in the Middle East, can further enhance the accuracy of the results. It was, however, not possible to repeat the physical examinations and pulmonary function studies during a possible later exacerbation of the children's illness, therefore, negative results of the examinations should be interpreted with caution, just as could be expected of a cross-sectional study.

The overall prevalence rates found in our study (Table 2) are not far from the reports of other urban populations.[11,12] Previous Persian studies from Tehran and Rasht have found the prevalence of current asthma and asthma with frequent attacks to be in the range of 5.3%-5.5% and 1%, respectively, for 6 years old children.[16] Their reported rates for the same findings in 14 years old children had risen to 9.7%-13.4% and 2.2%-2.3%, respectively.[16] The mentioned rates for current asthma are higher than our rates (4.4%), while the frequently recurring asthma in our series (1.6%) is closer to the Tehran and Rasht results. Also the increased prevalence of asthma with advancing age of the children as observed in our study, is in agreement with the reports from Tehran.[16]

The prevalence of previously diagnosed asthma in our series is disproportionately low (< 1%) compared to the reported symptoms of current asthma and even current severe asthma in this group. There are two different explanations for this finding; first one is misdiagnosis of asthma as viral bronchitis or pulmonary infections by the local general practitioners. The second, probably more important reason, may be the fear of the Persian parents of chronic diseases such as asthma, which inclines the physicians to use alternative descriptive terms such as allergy or hyper-reactivity to explain the situation to the parents. This kind of difference between asthma diagnosis and asthma symptoms has been reported from many other countries.[4,13,23,24] Some investigators have stressed the patients' lack of compliance or awareness to be an important reason for under-diagnosis of asthma,[24] as they believe that many patients fail to report more specific asthma symptoms to the physician.[24,25] Anyway, the difference between prevalence of true asthma and previously diagnosed asthma is more obvious in developing countries.[17,26] In our series the prevalence of persistent asthma, which causes conflicting effects on the child's life, like restricting sport activities and increasing school absence days, was 1.6%. This later rate which is somewhat close to the prevalence of diagnosed asthma may imply that the local practitioners label only the most severe cases as asthma, and less severe cases escape the exact labeling. The prevalence of disabling asthma has been reported to be at the level of 1.4% in the United States[8] which is close to our rates. However, the measured prevalence rates of asthma ever (7.6%) and current asthma (4.4%) are less than the rates reported from USA, Asian and European populations.[11,13,30]

With exception of the seven years old girls, there was always predominance of boys in our sample of chesty children. The male to female ratio for most of the asthma related symptoms was more than one; however, many times these differences were not statistically significant, and with increasing age of the children, the prevalence rates of the two genders became more equal. It should be noted that the equalization of the two ratios was not due to a decline of the prevalence of asthma in boys, but rather due to an increase in girls. Most authors have noted this male preponderance of childhood asthma.[27]

The unexpectedly high prevalence of asthma and related symptoms in seven year old girls in our series seems particularly odd and we have no explanation for this finding. We believe that this needs further epidemiologic evaluations.

It is noteworthy to mention that isolated recurrent cough among children without wheeze or shortness of breath appeared to have little relation to gender. The overall prevalence significantly decreased between the ages of seven and eleven years ($p < 0.001$), which is in agreement with the findings reported by other investigators.[28]

Despite the common belief,[29] the prevalence of asthma symptoms, current asthma and even the severity of asthma, did not improve with advancing age of the children in Isfahan. In fact the percentage of the involved children was higher in the older pupils than in the youngsters. Therefore, it can be noted that Isfahanian asthmatic children do not improve during maturation.

Such a tendency has been previously reported in some other parts of the world[27,30] and in Iran.[16] Nearly one fourth of the children (25.9%) were exposed to passive smoking at their homes; this rate is considerably less than those reported in industrial countries. The association between fathers smoking and asthma symptoms was significant ($p < 0.02$ by the χ^2 test) but the association vanished when the data were analyzed with logistic regression analysis. There was no correlation between respiratory symptoms and smoking mothers since there were only 59 smoker mothers in the series. It should be mentioned that many families reported that the smoker parent has stopped smoking at all or does not smoke at the household, after the physician's advice for the child's sake, which may explain the poor correlation between parental smoking and children's asthma.

The prevalence of wheeze ever and dyspnea ever increased with increasing ages of the students which seems to be due to an increased chance of exposure to initiating factors. Family history of asthma especially parental asthma, showed significant correlation with the prevalence of wheeze ever ($p < 0.02$), wheeze and shortness of breath ($p < 0.001$).

Presence of cockroaches in the household was associated with asthma and related symptoms ($p < 0.04$). Interestingly the commonly cited associations between asthma and the presence of pets in the western community households were not the same in Isfahan. In Isfahan, children only ownership of birds was significantly associated with asthma ($p < 0.008$), and dogs or cats could not be accused. It is noteworthy that pet ownership in Isfahan is quite different from the European countries and the United States, for example keeping a sheep in a yard in Isfahan is as odd as having a dog (Table 3). In fact, dogs and cats when present are usually not allowed to get into the living or bed rooms, and this may explain the lack of association between symptoms and these pets.

Our spirometric findings showed that post exercise FVC and FEV1 were not significantly affected by the presence of asthma symptoms; in fact only in 13 children (3.1% of the step 2), FEV1 was less than 80% of prediction. More sensitive parameters such as FEF25-75 and FEF 75,[2] were decreased to values of less than 70% of prediction in 44 (10.6%) and 88 (21.2%) of the tested pupils, respectively, while FEF25 and FEF50 were less affected. Residual volumes of more than 110% of prediction were recorded in 113 children (30.1%). The spirometric abnormal recordings were all significantly correlated with the more severe cases with frequent attacks ($p < 0.05$ for all parameters).

Airway resistance was higher than normal (0.196 kp/l/s = 2 cm H_2O) in 362 pupils (87.2%), and resistance levels of more than twice of that (> 0.4 kp/l/s) were still present in 259 pupils (63.2%). These rates seem to be exaggerated and unrealistic, therefore we believe that normal values for airway resistance need to be more standardized in Isfahan, and at present, measurement of resistance may lead to over diagnosis of asthma and is not recommended to be used for epidemiologic purposes.

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