

Prevalence of Asthma among Preschool Children in Edirne, Turkey

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SUMMARY Allergic diseases generally begin early during childhood, but a late diagnosis is common. This study aimed to evaluate the prevalence of asthma and asthma-related symptoms among kindergarten children in Edirne, Turkey. 873 subjects based on a modified ISAAC questionnaire were included. The prevalence of 'wheezing ever' and 'wheezing during the previous year' was 23.3% and 8.6%, respectively. Prior physician diagnoses existed for 36 of 873 (4.1%) children. The prevalence of children undiagnosed with asthma, but reporting asthma-related symptoms was 3.1%, 51.9% of which had previous β -agonist prescriptions. However, none of these children received inhaled anti-inflammatory medications. In conclusion, it was found that a large population of preschool children had undiagnosed respiratory symptoms suggestive of asthma. Conducting simple surveys of young children is particularly important, as identification of asthma early in the disease course will facilitate effective prevention and treatment.

Asthma is the most common chronic childhood disease. Over the last several decades, its worldwide prevalence has increased rapidly. A number of surveys have determined the prevalence of this disease by using questionnaires, spirometry, and assessment of airway hyperresponsiveness. To facilitate a comparison between centers, the International Study of Asthma and Allergies in Childhood (ISAAC) investigative group has developed a standardized questionnaire for describing the prevalence of childhood asthma and allergic disease.¹

A previous study of children aged 13-14 years utilized the ISAAC questionnaire. It included data from 56 countries and found that the prevalence of wheeze in the previous 12 months was within a range of 2.1 to 32.2%.²⁻³ A similar prevalence of wheeze (4.1-32.1%) was reported in a study of six to seven year old children from 38 countries.³ Studies from different regions of Turkey that utilized the ISAAC questionnaire found that the prevalence of

wheezing in the last 12 months ranged from 4.7 to 14.7% among children aged six to 18 years.⁴⁻⁸

Physician reports, current disease, and wheezing are usually taken into consideration when determining the prevalence of asthma based on questionnaires. However, several studies have reported that parents often confuse wheeze with other respiratory sounds.⁹ This may lead to inaccurate estimations of the true prevalence of wheeze. Thus prevalence studies often use the rate of physician-diagnosed asthma. A study by Rönmark *et al.*¹⁰ validated questionnaire data through structural interviews with the parents of symptomatic children. The study found a high specificity (> 99%) for the question "Has your child been diagnosed as having asthma by a physician?". The sensitivity in the Rön-

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mark study was around 70%. Another study by Remes *et al.*¹¹ validated the symptom questionnaire by tests of bronchial hyperresponsiveness (BHR). This study found that despite their high specificity (> 97%), BHR tests did not significantly improve the diagnostic accuracy compared to symptom history.

Allergic disorders usually manifest in the early childhood, but often go undiagnosed until later in life. However, early diagnosis of asthma facilitates effective prevention and treatment. The diagnosis of asthma in preschool children is a challenge for both clinicians and epidemiologists. There are several wheezing phenotypes in early childhood. Some of these phenotypes develop into atopic asthma, while others are transient conditions.¹² The present study aimed to investigate the prevalence of asthma and asthma-related symptoms in kindergarten-age children. Few studies have addressed asthma screening in the preschool age group.¹³⁻¹⁷ This is the first study to present such data from Turkey.

SUBJECTS AND METHODS

The basis of this study was a standard written questionnaire evaluating the symptoms of asthma, and the verification of questionnaire responses through telephone interviews. This study was a part of a larger study that examined the prevalence of allergic diseases in Edirne's city center. The study, conducted between December 2003 and May 2004, utilized a cross-sectional design. Study subjects returned all questionnaires within one of month of distribution. Only children whose parents completed and signed both the consent forms and questionnaires were included in the study.

Subjects

The subjects were children between one and six years old, who attended nursery, kindergarten and preparatory classes of elementary schools in the city center of Edirne. The Ethics Review Committee at the Trakya University Medical Faculty approved this study. After receiving permission from the Department of National Education in Edirne, a research assistant from the study team visited each kindergarten, delivering study packages to the schools' directors for distribution to the children. Study packages included an introductory letter for the families, a pa-

rental consent form, and the ISAAC questionnaire. The school system reported that approximately 1,086 children received the packages.

Questionnaire

ISAAC core questions developed for six to seven year old children were used to assess the prevalence and severity of respiratory symptoms, provoking factors, diagnoses and medical treatments.¹ These were supplemented by validated questions from other published papers,^{13,14,18} with slight modifications (detailed shown in Table 3). Additional questions included family occupations, monthly incomes, health insurance coverage, and the name and relationship to the child of the person who completed the questionnaire. The consent forms fully explained the nature and aims of the study.

Before distributing the questionnaire, it was tested on 30 parents in our outpatient clinic. Frequently misinterpreted questions were identified through interviews with the parents and reworded for use in the study.

Structured interview

All individuals who responded affirmatively to at least two cough symptom questions, or who responded positively to any other asthma symptoms, as well as subjects with a previous asthma diagnosis were selected for a structured telephone interview. One specially trained research assistant conducted all telephone interviews. Three call attempts were made to each respondent, including home and work phones.

Those subjects who answered question 9 affirmatively and had a physician's diagnosis of asthma were recognized as asthmatics. Those who reported wheeze in the past year, in combination with at least one of the asthma symptom questions in the past year (questions 4-8) were considered as asthma-related symptoms cases.

Statistical analyses

All statistical analyses were performed using MINITAB release 13.32 statistical software (MINITAB Inc. US). Descriptive statistics were expressed

as mean \pm SD, median and range. Prevalence rates were calculated between 95% confidence interval (CI) values. Categorical data were tested using chi-square statistics.

RESULTS

Parents returned 82.7% of the 1,086 questionnaires distributed at schools. Twenty-five of these were returned empty, bringing the total number of questionnaires included in the study to 873. Tables 1 and 2 show the sample demographics. In 65.5% of the cases the child's mother responded (572/873), and in 13.1% (114/873) the father. In 20% of the cases (175/873), both parents completed the questionnaires. The families of 145 children (16.6%) earned low incomes, and 67 (7.6%) had no health insurance.

The telephone interview process uncovered inappropriate responses to questions in 23 cases (2.6%). These survey errors were corrected before performing data analysis.

Table 3 shows the prevalence of asthma and asthma-related symptoms. Twenty-three percent of the respondents reported that their child had wheezed at some time in its life, with 8.6% reporting wheezing in the last 12 months. Dry cough at night during the last 12 months was the most common symptom (19.0%). Respondents reported physician-diagnosed asthma in 4.1% (36/873) children. Bronchitis was the most commonly reported respiratory illness (266/873, 30.5%) (Table 4).

The asthma severity assessment included the frequency of wheezing attacks, sleep disturbance, speech disturbance or difficulty in feeding, acute care visits or hospitalizations, and nocturnal cough

(Table 5). Of 873 children, 1.2% reported nocturnal wheeze that caused sleep disturbances at least once a week in the past year. Seventeen subjects (1.9%) reported speech disturbance or limitation of feeding due to shortness of breath. Twenty-one (2.4%) needed emergency treatment or hospitalization because of wheezing during the last 12 months. Frequent nocturnal cough (two or more days a week) during the past year was reported in 2.5% (22/873) of the subjects.

Following the evaluation of the questionnaires and the telephone interviews, the 36 (4.1%) subjects with physician diagnoses were accepted as asthmatic. Twenty-seven subjects (3.1%) had asthma-related symptoms, but were previously undiagnosed. Among the asthma-related symptom subjects, 51.9% (14/27) had nocturnal dry cough in the last 12 months. The reported prevalence of severe cough, shortness of breath and chest tightness during or after exercise, and wheezing during or after exercise during the previous year was 48.1% (13/27), and 26.9% (7/27), respectively. Among the children with physician-diagnosed asthma, the prevalence of noc-

Table 1 Age distribution of the sample population (n = 873)

	N	%
Age (years)		
1	2	0.2
2	9	1.0
3	89	10.2
4	266	30.5
5	503	57.6
6	4	0.5
Total	873	100

Table 2 Demographic characteristics of children aged 3 to 5 years

Age (years)	Gender				Indoor tobacco exposure		Low family income		Health insurance		Parental history of atopy		Total no.
	Female		Male		n	%	n	%	n	%	n	%	
	n	%	n	%									
3	49	55.1	40	44.9	6	6.7	4	4.5	82	92.1	9	10.1	89
4	121	45.5	145	54.5	16	6.0	36	13.5	255	95.9	43	16.2	266
5	263	52.3	240	47.7	38	7.6	10	2.0	454	90.3	64	12.7	503

tural dry cough, severe cough, shortness of breath and chest tightness during or after exercise, and wheezing during or after exercise during the previous year was 41.7% (15/873), 38.9% (14/873), and 20.0% (7/36), respectively. These numbers were not significantly different from those of the cases with asthma-related symptoms ($P = 0.42, 0.46, \text{ and } 0.53$, respectively). Other asthma symptoms and the parameters relating to asthma severity were similar between previously diagnosed asthma cases and asthma-related symptom subjects.

β -agonists were the most commonly used

medications, with 18.1% of 873 subjects reporting their use in the last 12 months. The proportion of respondents who reported using other asthma medications in the last year, including sodium cromoglycate and corticosteroids, was 1.7% (15/873) (Table 6). Among asthma-related symptom subjects, 14 cases (51.9%) reported prior use of a bronchodilator. However, none reported using prophylactic asthma medications. Over 60% of those symptomatic but undiagnosed subjects reported respiratory diseases such as bronchitis or bronchiolitis. The use of bronchodilator drugs was reported in 72.2% (26/36) of physician-diagnosed asthma cases. Twenty-three

Table 3 Prevalence of asthma and asthma symptoms

Question	n	%	CI
Symptoms			
Has your child ever wheezed?	203	23.3	20.5 - 26.2
In the last 12 months, has your child ever wheezed?	75	8.6	6.8 - 10.7
Has your child ever had a cough that lasted more than 3 weeks?	93	10.7	8.7 - 12.9
In the last 12 months, has your child ever had a cough that lasted more than 3 weeks?	58	6.6	5.1 - 8.5
Has your child had a dry cough at night, apart from a cough associated with a cold or a chest infection in the last 12 months?	166	19.0	16.5 - 21.8
In the last 12 months, has your child ever had wheezing during or after physical activity?	18	2.1	1.2 - 3.2
In the last 12 months, has your child ever had cough, chest tightness or shortness of breath during or after physical activity?	80	9.2	7.3 - 11.3
In the last 12 months, has your child ever had a severe nocturnal cough, shortness of breath or chest tightness?	55	6.3	4.8 - 8.1
Asthma ever			
Has your child ever been diagnosed as having asthma by a physician?	36	4.1	2.9 - 5.7

Table 4 Prevalence of respiratory illnesses

Question	n	%	CI
Has your child ever been diagnosed as having any of the following illness by a physician?			
Pneumonia	62	7.1	5.5 - 9.0
Bronchiolitis	57	6.5	5.0 - 8.4
Bronchitis	266	30.5	27.4 - 33.6
Whooping cough	7	0.8	0.3 - 1.7
Croup	55	6.3	4.8 - 8.1
Sinusitis	110	12.6	10.5 - 15.0

(63.9%) physician-diagnosed asthma cases reported using prophylactic asthma medications in the last 12 months. Over 92% of the families with previously diagnosed cases and asthma-related symptom subjects had health insurance, and their monthly household incomes did not differ significantly.

DISCUSSION

The present study assessed the prevalence of asthma and asthma-related symptoms among 873 young children in Edirne's city center. To our knowledge, this study was the first to investigate the prevalence of asthma among kindergarten-age Turkish children. When symptoms related to asthma such as 'wheezing ever' were considered, our prevalence

was 23.3%, which was higher than other surveys conducted in Turkey.⁴⁻⁸ When wheezing in the last 12 months was considered, our prevalence rates resembled those of Istanbul (8.2% and 7.2%).^{4,6} However, the differing age groups of the study subjects limited a direct comparison of our study with published work from other regions of Turkey. Other questionnaire-based surveys, conducted outside of Turkey, described the prevalence of wheezing symptoms among one to six year-olds. These surveys reported the prevalence of 'wheezing ever' and 'wheezing in the last 12 months' as varying between 15.6 – 29.0% and 13.0 – 30.8%, respectively.¹³⁻¹⁶

Some limitations in the present study require acknowledgement. Parents often confuse wheeze

Table 5 Severity of asthma symptoms in the last year

Question	N	%
Number of wheezing attacks in the past year		
0	789	91.3
1- 3	55	6.3
4-12	15	1.7
> 12	5	0.6
How often sleep was disturbed due to wheezing in the past year		
Never	848	97.1
< 1 night/week	10	1.1
1 - 2 nights/week	3	0.3
> 2 nights/week	7	0.8
An episode of wheezing so severe that child was only able to say 1 to 2 words between breaths or refused feeding	17	1.9
Number of visits to emergency room or hospitalizations for wheezing in the past year		
None	848	97.1
1-3	14	1.6
4- 8	7	0.8
9-11	-	-
12+	-	-
Frequency of nocturnal dry cough apart from a cough associated with a cold or a chest infection in the past year		
None	703	80.5
A few times per month	125	14.3
Two or more days a week	22	2.5
Daily	-	-

with other respiratory sounds.⁹ The Turkish language has no equivalent word for 'wheeze.' The word 'wheeze' is frequently translated as 'a whistling sound coming from the chest'. However, parents may perceive any sound coming from the upper airway as wheeze. Further, questionnaires might have been returned either incomplete or filled out incorrectly, as reported by Gruchalla *et al.*¹⁹ In our survey, 2.6% of the questionnaires were incorrectly filled out. We were also confronted with the lack of an established gold standard for detecting asthma.¹⁸ Because of these problems, some previous studies validated questionnaires through physical examinations^{10,11,18,20,21} and objective measurements such as specific IgE, skin prick tests, pulmonary function tests,^{9-11,19,20} or assessment of bronchial hyperresponsiveness.^{11,19} While airway hyperresponsiveness is one of the most characteristic features of asthma, hyperresponsive airways are not sensitive or specific enough for a reliable asthma diagnosis.²²

In our study, we verified questionnaire data through telephone interviews. To reduce survey errors due to instrument decay, the same trained research assistant conducted each interview. In most cases, asthma could be diagnosed with reasonable accuracy by taking a careful symptom history, as reported by Remes *et al.*¹¹ However, it is now well rec-

ognized that there are several wheezing phenotypes in early childhood. Some of these develop into atopic asthma, while others are transient conditions.¹² Our study accepted as asthmatic those subjects previously diagnosed with asthma by a physician. Asthma-related symptom subjects included those who reported symptoms that are frequently associated with asthma during the previous year, without having a physician's diagnosis of asthma.

While selecting asthma-related symptom subjects, we included subjects who had wheeze during the last year in combination with at least one positive response to cough-related or exercise-related symptoms. Nocturnal coughing is a very sensitive sign of asthma. However, it may lack specificity to asthma.¹³ In our study, 19% of the respondents reported dry cough at night in the last 12 months. Conversely, a chronic cough may be due to asthma.²³ Therefore, we chose to include coughing lasting more than three weeks in our questionnaire. For a better selection of asthma-related symptom subjects, other cough-related questions added into our questionnaire were severe nocturnal cough, chest tightness and shortness of breath. Exercise-related symptoms included exercise-induced wheezing, exercise-induced coughing, chest tightness, and shortness of breath.

Table 6 Asthma medication use in the last year

Question	N	%
Asthma medication used in last 12 months		
β-agonist (Ventolin or Bricanyl in spray, liquid, nebuliser form)		
Not at all	715	81.9
< 4 times	133	15.2
4-12 times	18	2.1
> 12 times	7	0.8
Corticosteroids or sodium cromoglycate (Intal, Becotide, Becloforte, Pulmicort in spray, dry powder inhalers, discus, nebuliser form)		
Not at all	855	97.9
< 4 times	5	0.6
4-12 times	5	0.6
> 12 times	5	0.6

In our study, 36 (4.1%) respondents reported a previous physician diagnosis of asthma of their children. All of those cases had symptoms consistent with asthma. Studies from different regions of Turkey that utilized the ISAAC questionnaire found that the prevalence of physician diagnosed asthma ranged from 4.0 to 14.1% among children aged six to 18.⁴⁻⁸ The age ranges of the study groups differed from those in our study. However, our study's prevalence of physician-diagnosed asthma was similar to the result of a survey conducted by Akcakaya *et al.*⁷ in Istanbul. The prevalence of previously physician-diagnosed asthma in our survey was generally lower than that described in questionnaire-based surveys conducted in other countries.¹³⁻¹⁷

We found that 3.1% of the preschool children had not received formal asthma diagnoses, yet they reported symptoms that were suggestive of asthma. In two other surveys of preschool children, reported by Grant *et al.*¹³ and Berg *et al.*¹⁷ the prevalence of asthma-related symptoms unassociated with a diagnosis of asthma was 30.1%, and 6.6%, respectively. However, the survey methodology was different. In the present study, the reported prevalence of asthma symptoms, or the parameters relating to asthma severity, were not different between symptomatic undiagnosed subjects and previously diagnosed asthma cases. Use of β -agonists in the last year was reported in 72.2% of previously diagnosed asthma cases, and in 51.9% of the asthma-related symptom subjects ($P=0.097$). Twenty-three (63.9%) of those diagnosed asthmatics used anti-inflammatory medications in the last year. However, none of the undiagnosed cases with asthma-related symptoms reported previous use of prophylactic asthma medications. Bronchodilator drug prescriptions may relate to the diagnosis of bronchitis or bronchiolitis.

Acute bronchiolitis is a common disease of the lower respiratory tract in infants, resulting from inflammatory obstruction of the small airways. Bronchiolitis is seasonal, with a peak activity during winter and early spring. Acute bronchiolitis is predominantly a viral disease. Respiratory syncytial virus (RSV) is responsible for more than 50% of the cases.²⁴ Clinicians should diagnose bronchiolitis and assess disease severity on the basis of history and physical examination.²⁵ The illness is usually preceded by exposure to an older contact with a minor

respiratory syndrome within the previous week. The infant first develops a mild upper respiratory tract infection with sneezing and clear rhinorrhea. This may be accompanied by diminished appetite and fever of 38.5–39°C (101–102°F), although the temperature may range from subnormal to markedly elevated. Gradually, respiratory distress ensues, with paroxysmal wheezy cough, dyspnea, and irritability. The physical examination is characterized most prominently by wheezing. Auscultation may reveal fine crackles or overt wheezes, with prolongation of the expiratory phase of breathing. The condition most commonly confused with acute bronchiolitis is asthma. The two conditions may not be distinguishable during the first episode, but repeated episodes of wheezing, absence of a viral prodrome, and presence of a family history of atopy or asthma supports a diagnosis of asthma. Bronchodilators produce modest short-term improvement in clinical features, but the statistical improvement in clinical scoring systems seen with them is not always clinically significant.²⁴

Chronic bronchitis (CB) in adults is defined as a disorder manifested by a chronic or recurrent productive cough present on most days for three months a year for two years. In contrast a clear definition, etiology, natural history, therapy, and prognosis have not been described for in childhood. Morgan *et al.*²⁶ defined it as the symptom complex of chronic (> 1 month) or recurrent productive cough that may or may not be associated with wheezing or crackles on auscultation. The symptomatic child with reactive airways will be diagnosed asthma or wheezy bronchitis. In contrast, the child with less reactivity but more mucus production may develop a prolonged productive cough and fall into the CB category. Thus, asthma and CB have considerable overlap and may only be differentiated by how much acutely reversible air narrowing is present at the time of diagnosis.²⁶

Asthma is a disease characterized by (1) hyperresponsiveness of bronchi to various stimuli, and (2) changes in airway resistance, lung volumes, and expiratory flow rates, with symptoms of cough, wheezing dyspnea, or shortness of breath.²⁷ Measurements of lung function provide an assessment of the severity, reversibility, and variability of airflow limitation, and help confirm the diagnosis of asthma in patients older than 5 years. An increase in FEV1

of 12% (or ≥ 200 ml) after administration of a bronchodilator indicates a reversible airflow limitation consistent with asthma. Most children who develop wheezing after age 5 have asthma. However, diagnosis of asthma in children 5 years and younger presents a particularly difficult problem. In children 5 years and younger, the diagnosis of asthma has to be based largely on clinical judgment and an assessment of symptoms and physical findings. A useful method for confirming the diagnosis in this age group is a trial of treatment with short-acting bronchodilators and inhaled glucocorticosteroids. Marked clinical improvement during the treatment and deterioration when treatment is stopped supports a diagnosis of asthma.²⁸

The physicians' limited understanding of the diagnostic criteria of childhood asthma, or familial concerns about an asthma diagnosis might be the reason for frequent diagnoses such as bronchitis or bronchiolitis instead of asthma. Similarly, previous studies have also documented a mismatch between children with an asthma diagnosis and children with prescriptions for asthma medications.²⁹⁻³⁰

In conclusion, our study has limitations related to questionnaire-based, self-administered surveys. Specifically, we were concerned with self-selection bias among respondents and instrument decay. Follow-up phone calls controlled for self-selection, and using the same research assistant to conduct each call controlled for instrument decay. In our study, 3.1% of preschool children had undiagnosed respiratory symptoms suggestive of asthma. We believe that utilizing questionnaire-based surveys represents a cost-effective method of prescreening large numbers of children for symptoms suggestive of asthma. We suggest that preschool children reporting frequent asthma-related symptoms be referred for further evaluation and prompt treatment by a physician.

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