The cost of childhood asthma and its determinants in Ankara, Turkey*

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Bronchial asthma is one of the most common chronic diseases of childhood. In recent years a consistent increase in the prevalence, and concomitantly, in the social and economic impact of the disease, has been reported.

In order to provide data for the cost of pediatric asthma and its determinants in Turkish children, a study was performed in a single outpatient clinic, which encompasses a questionnaire-guided interview and retrospective evaluation of the last year files.

From the 183 patients enrolled, most were males (65.6%) and atopics (63.5%), with a disease severity of mild intermittent (67.7%). Mean annual total costs per patient was US$991.7±73.2 (median=688.8) and the largest proportion of the direct costs was due to outpatient clinic costs (48.5%). Mean cost of any hospitalization per patient was US$955.5±16.5. In multivariate analysis, the disease severity, current use of preventive drugs and current use of emergency sevice and/or current hospitalization appeared to be the main determinants of direct costs.

Adequate control of the disease plays a key role in decreasing the total direct costs of pediatric asthma although it increases the medication and outpatient costs.

Key words: asthma, disease burden, childhood, cost, determinant.

Bronchial asthma is the most common chronic disease of childhood. In recent years, a consistent increase in the prevalence of asthma has been reported from various regions of the world[1]. Concomitantly, the social and economic impact of the disease is also increasing[2-19].

Pediatric asthma accounts for a large proportion of childhood hospitalizations, physician visits, absenteeism from school and parental absence from work. Numerous factors affect the costs of childhood asthma, like disease severity, undertreatment, inadequate preventive drug use and inadequate medication regimens, exposure to environmental agents and lack of education of patients, families and caregivers[1,6,9]. The attitude of physicians, cost of asthma medications, especially for exporting countries, frequency of the use of laboratory settings, and expectations of physicians and patients are other potential contributing factors[20]. The knowledge of the cost of asthma is especially valuable in documenting the burden of the disease, in developing strategies for management and health economics and, potentially, in increasing physician awareness. To date, there have been relatively few studies performed regarding the cost of childhood asthma, and the available information has been gained mostly from studies conducted in western countries[8,10,13,18,19]. To our knowledge, there is no study attempting to document the cost of pediatric asthma in Turkey. Here, we report the results of a survey that attempted to estimate the cost of asthma and the determinants in a group of Turkish children to document the economical burden and to facilitate international comparisons. Our observations form the basis of the present report.

** This study was conducted as the public health specialty thesis of NEB.*

Material and Methods

Subjects

The study was performed in the outpatient clinic of the Pediatric Allergy and Asthma Unit of Hacettepe University İhsan Doğramacı Children's Hospital, which is the largest pediatric asthma outpatient clinic of the country. While the clinic serves as a referral center for the entire country, patients may also admit upon request; thus, it functions as both a primary and tertiary health care service. Asthmatics are usually seen two or three times a year at scheduled visits, but unscheduled visits are also permitted whenever required. The study was performed during a randomly selected three months (May, July and September 2004) and from eight physicians of the clinic, four accepted to refer their patients to the investigator. All of the asthmatic children aged 3 to 16 years with scheduled or unscheduled visit were invited to participate in the study; no other sampling frame was used. All patients had a history of recurrent wheezing and dyspnea and had been diagnosed as having asthma. All were documented to have reversible airway obstruction either clinically and/or with pulmonary function tests. Other obstructive airway disorders were excluded by relevant investigations if required. Atopy was defined as at least one positive skin prick test (3 mm greater wheal from negative control in the presence of flare reaction) to a panel of 20 common aeroallergens, in the presence of positive and negative controls. Generally, all subjects had been skin-prick tested at their first scheduled visit and this was repeated every 2-4 years to determine any change in sensitizations. Results of the final skin prick test were recorded for the study.

Study Design

The study was composed of two parts: The first included a questionnaire filled by the investigator (NEB) and elicited data on demographics of parents and patients, frequency of bronchial symptoms, triggers, treatments, satisfaction from treatment, perception of physician's approach and impact of asthma on daily life. Questions, aside from demographics and frequencies, were prepared as statements and answered on a scale with minimum and maximum scores of 1 and 4 in order to reflect patients'/caregivers' perceptions. Following the demographic questions, they were queried regarding the treatments they had received during the last year either for asthma or comorbid diseases including medical equipments (i.e. nebulizer, peak flow meter, influenza vaccination, and immunotherapy), ambulance usage, and transportation and hotel costs. Thereafter, patients/caregivers were questioned regarding their educational background, smoking habits, the characteristics of their local physician, loss of work days due to their child's asthma, and use of complementary/alternative medicine for their child's asthma.

The second part of the study was a retrospective analysis of files to document the severity of asthma as perceived by physicians, allergies, treatments and the direct costs incurred at the clinic during scheduled/unscheduled visits and emergency/hospital admissions. The cost data derived from the expenditures of the last one year period (current costs) prior to the outpatient clinic admission at which the questionnaire had been applied. All of the costs mentioned in the study were those directly due to asthma within the last one year period prior to the interview. All cost items of the last year were examined and those not related to asthma were excluded. Unfortunately, collection of the data concerning direct costs was limited primarily to our clinic because of unavailability of the cost data of other health services. In order to estimate the yearly cost, unavailable data were adjusted as the mean of the available data. For instance, if there was no data for the cost of any one emergency visit, then the mean cost of other emergency visits was used as the cost of that visit.

The costs were divided into direct and indirect costs. Direct costs were further categorized as direct medical costs and direct non-medical costs. Direct medical costs included costs of outpatient clinic visits, emergency visits, hospitalizations, and prescriptions (medication costs apart from hospital). Direct non-medical costs were transportation for medical care, housekeeping assistance, private school (if govermental school was not preferred because it was considered to be less safe due to environmental exposures and less teachers' assistance), household fixings and allergen control measures (special basement, air cleaners, special vacuum cleaners, anti-allergic bed covers, anti-allergic beds) and alternative/

complementary/traditional treatment costs. Indirect costs, which included lost work productivity, lost full work days of parents and loss of other productivities, were not assigned a monetary value because in Turkey an individual's daily income fluctuates, and government employees do not forfeit their daily income when they miss work days. Therefore, it would not have been meaningful to assign a monetary value to such costs. However, we did consider the lost work days (number of days), school absenteeism of the patient (number of days), and the degree of the effects of asthma on a patient's school life and daily activity and parents' work life.

Questionnaire

The 45-item questionnaire was prepared by the investigators based on the information available in international asthma guidelines. The questions were partially adapted from the previous studies with some modifications[5,21]. The questionnaires were validated on a sample of 10 patients through 10 in-depth interviews. All the interviews with parents were conducted in the presence of children who supplied information that the parents were unable to provide (e.g. severity of symptoms). Time to complete the questionnaire was usually between 15-20 minutes.

Statistics

The statistical relations between direct costs and socio-demographic factors, disease severity, and indirect costs were determined by independent samples t-test, one-way ANOVA test, and the Tukey Honestly Significantly Different test as univariate analyses. After univariate analyses, binary logistic regression was used to determine the effects of some factors on the direct costs. In order to apply logistic regression, direct costs were divided into two according to the median value in order to convert the continuous variable into a dichotomous variable. The 95% confidence interval (CI) was chosen to flag the significance. Variables that were associated with the outcomes in the univariate analysis at a p value of less than 0.25 were examined in the multivariate logistic regression models. A backward reduction modelling strategy was used. Backward elimination started with all of the variables in the model. Then, at each step, variables were evaluated for entry and removal. The score statistic was always used for determining whether variables should be removed from the model. Wald statistic was used to select variables for removal (by default 0.10). The size of the effect of each of the risk factors was measured by using the odds ratios (ORs) and 95% CIs. Statistical analysis was done using the SPSS 11.5 package program (SPSS, Inc, Chicago, IL, USA).

Ethical Issues

All parents provided written informed consent to participate in the trial, which was approved by Hacettepe University's Ethics Committee. Verbal and written consents of children under or over 10 years of age, respectively, were also obtained.

Results

During the study period, a total of 521 asthmatic children admitted to the outpatient clinic; 202 patients (38.7%) were the subjects of the study because they were seen by the four physicians who accepted to refer their patients for the study. From 202 asthmatic patients, 7 refused to participate (response rate=96.5%) due to time limitation and/or unwillingness to document income/expenses. Because of the lack of cost data, a further 12 patients were excluded from the study. Finally, the statistical analyses were done including 183 patients (participation rate=90.5%) in order to examine the cost of childhood asthma and its determinants.

Most of the outpatient visits (scheduled/unscheduled) (61.6%) and some extent of emergency visits (43.6%) were conducted in the study center; other health care facilities were used in 39.4% (n=751) of cases for outpatient and in 56.4% (n=78) for emergency visits. There were eight hospitalizations, only two of which occurred in the study center.

Study Population

Table I shows the characteristics of the 183 patients involved in the study and their parents. There were twice as many male participants as female and the mean age of study population was 9±3 years. Most had mild intermittent disease (67.7%) and according to the file records, 18% and 2.7% of the patients had allergic rhinitis and atopic dermatitis,

Table I. Characteristics of the Study Population

Characteristics	Frequency (n=183)		
	N	%	CI
Gender (Male)	120	65.6	56.2-75.0
Age			
3-6	52	28.4	24.4-32.4
7-11	75	41.0	35.2-46.8
12-16	56	30.6	26.3-34.9
Parental education			
Both below high school	15	8.2	0.05-0.11
One of them high school or higher	51	27.9	27.6-28.2
Both high school and higher	117	63.9	63.6-64.2
Annual family income (n=174)			
≤$750	100	57.5	49.3-65.7
>$750	74	42.4	36.4-48.4
Disease severity			
Mild intermittent	124	67.7	58.0-77.4
Mild persistent	36	19.7	17.0-22.4
Moderate or severe persistent	23	12.6	10.9-14.3
Comorbid diseases			
Allergic rhinitis	33	18.0	15.5-20.5
Atopic dermatitis	5	2.7	2.5-2.9
Mother's asthma	13	7.1	6.2-8.0
Atopy	115	63.5	54.4-72.6
Indoor smoke	43	23.5	20.2-26.8

respectively. Almost 63.5% were atopics, and grass pollen (37.6%) and house-dust mite (31.5%) were the most commonly sensitized allergens. The mean age of asthma diagnosis was 4.7±0.2 years (median=4.0).

Current use of emergency care was 24.0% (at least one admission to emergency health care service within the last one year). The current and ever hospitalization rates were 4.4% (n=8) and 29.0% (n=53), respectively. The mean numbers of current hospitalization and use of emergency service were 0.06±0.02 and 0.4±0.01, respectively, for the study group. Mean admission number (scheduled/unscheduled) to any health care facility for asthma during the last year was 4.1±0.3. For those children who were only using the study center, the current rates of emergency care use and hospitalization were 15.3% and 0.8%, respectively, and these rates were lower than the rates of the entire study population ($p<0.01$).

As expected, fathers were more educated than mothers, with 65.6% of mothers having an educational status of high school or above, versus 90.2% for fathers. According to the parental declaration, 7.1% of the mothers and 2.7% of the fathers had been diagnosed as asthma. Indoor smoking was reported as 23.5% of the study population. The mean family income of the study group was US$907.5±45.2/month.

In the study population, asthma caused current school absenteeism at a mean of 12.3±2.5 days per academic year and it was more prominent in children with moderate to severe disease (32.8±11.9 days/year). Working mothers and fathers reported a mean of 3.5±0.5 and 3.6±0.6 lost work days during the last year, respectively.

Buying of anti-allergic cushions, special basements, vacuum cleaners and anti-allergic beds were reported in 18.6%, 4.9%, 6% and 7.7% of the families, respectively. Interestingly, 15.3% and 4% of patients without dust-mite allergy (n=124) had purchased anti-allergic beds and special vacuum cleaners, respectively. Use of alternative/complementary medicine during the last year was noted in 24.6%; herbal teas, honey and quail eggs were the most commonly used treatments.

Direct Costs

Direct costs are summarized in Table II; mean annual total cost per patient was US$991.7 ±73.2 (median= 688.8).

a) Direct Medical Costs

The largest proportion of the direct costs was due to outpatient clinic costs (48.5%), and the mean total cost of one visit in an outpatient clinic was US$120.2±5.6. The majority (75.8%) of outpatient costs were due to laboratory examinations such as pulmonary function tests (44.0%) and skin prick test (34.0%), and almost 20% of the outpatient clinic costs belonged to the physician's cost. The emergency visit costs were only 2.8% of the total costs and mean emergency cost per one admission was US$72.0 ±5.8. The costs for patients who admitted only to the study clinic (outpatient and/or emergency) was US$666.3±45.5, and this was lower than the mean cost of the whole group ($p<0.05$).

Of the study population, 73.8% and 69.9% reported current use of short-acting ß2 agonists and preventive drugs [inhaled corticosteroid (ICS), leukotriene receptor antagonists (LTRA), beta-2/ICS combination], respectively. Of patients who did not report current use of preventive drug, 83.6% had an asthma severity of mild-intermittent. The cost of preventive drugs accounted for 15.2% of the total costs.

More than one-third of patients (37.2%) had been vaccinated for influenza during the last year, accounting for a mean cost of US$12.3±0.3 per patient (mean cost per vaccinated patients). The total costs of medical equipment like nebulizers, spacers and peak flow meters accounted for US$5.7±1.2 per patient for the whole study group.

In the study group, seven patients had first-time diagnosis of asthma, and the mean cost of this diagnostic work-up was US$198.5±28.8, suggesting that cost of diagnostic work-up is more than that of routine follow-up or unscheduled or emergency visits ($p<0.01$ for each).

Eight patients had been hospitalized within the last year, and the mean hospitalization cost per patient was US$955.5±16.5, of which laboratory examinations accounted for 70.1% of total hospitalization costs (US$670.4±130.5). From the eight patients hospitalized within the last year, two had mild-intermittent, two mild-persistent, and four moderate to severe persistent asthma.

Table II. Direct Annual Costs Caused by Asthma Per Patient (n=183)

	Annual Costs (US$) Per Patient			
Source of cost	Mean±SEM	Range	Median	% Total
Medical costs				
Outpatient clinic visits	481.5±42.7	9.5-5843.4	320.8	48.5
Emergency visits*	118.6±11.4	16.9-359.9	76.9	2.8
Hospitalization**	955.5±16.5	372.6-2097.9	693.3	4.2
Medication				
Short-acting ß2-agonists	28.1±3.6	0.0-406.0	12.9	2.8
Preventive drugs	150.7±17.2	0-1351.6	53.6	15.2
Antihistamines	7.1±1.0	0.0-113.2	0.0	0.8
Oral-i.v. corticosteroids	0.3±0.1	0-27.7	0.0	0.1
Nasal corticosteroids	8.3±1.2	0.110.4	0.0	0.9
Influenza vaccination	4.5±0.4	0.0-22.9	0.0	0.5
Medical equipment	5.7±1.2	0.0-108.0	0.0	0.6
Alternative/complementary therapy	16.1±4.4	0.0-529.4	0.0	1.7
Non-medical costs				
Transportation	87.7±7.5	0.0-458.8	58.8	8.8
Home care	46.7±21.5	0.0-3088.2	0.0	4.7
Household fixings and allergen control measures	62.0±14.7	0.0-1323.5	0.0	6.2
Hotel costs	21.9±4.5	0.0-441.1	0.0	2.2
Total	991.7±73.2	89.4-8724.7	688.8	100.0

*Mean cost of an emergency visit (n=44).
**Mean cost of a hospitalization (n=8).

b) Direct Non-medical Costs

Of the study group, only 43.2% lived in Ankara, where the clinic is located. The remaining 56.8% of the patients were living in other cities of Turkey, resulting in a mean transportation cost of US$150.2±9.5 per patient annually. Although in 10.5% of the patients, there were pediatric allergists in the city in which they lived, they reported a preference to be treated in the study clinic as it is the one of the most experienced in the country. Taken together, 11.4% of the mean total costs were due to transportation. Hotel costs of patients and parents/caregivers during the time of therapy and examinations were US$37.8±7.6 per patient annually. Six families (3.2% of whole group) employed a regular housekeeper within the last year to take care of the asthma patient. The costs of special home care (keeping a regular housekeeper) for this group and the whole study population were US$1424.6±348.8 and 46.7±21.5 per patient, respectively. Cost of household fixings and allergen control measures within the last year was US$62.0±14.7 per patient in the study group.

Determinants of Direct Costs

Univariate analysis of potential variables for the total cost of asthma and the effect of disease severity on the total direct costs are summarized in Tables III and IV. According

Table III. Univariate Analysis of the Variables for the Direct Cost of Asthma

Determinants	N	Mean±SEM (US$)	P	CI
Gender			0.95	-295.4 – 314.4
Male	120	994.9±82.1		
Female	63	985.5±145.1		
Age			0.04	4.5 - 626.4
3-12	127	1088.2±98.2		
>12	56	772.7±80.8		
Parental education			0.34	-155.9 – 445.9
One of them below high school	66	1084.4±147.9		
Both of them high school or higher	117	939.4±78.5		
Comorbid allergic disease			0.13	-73.3 – 540.1
Yes	60	834.8±85.6		
No	123	1068.2±100.1		
Asthmatic mother			0.38	-1141,4 - -26.5
Yes	13	1354.2±640.7		
No	170	950.2±61.9		
Atopic			0.69	-243.4 – 364.4
Yes	115	973.7±103.3		
No	66	1034.2±94.2		
Exercise symptoms			<0.01	-686.1 - -139.6
Yes	98	1183.5±120.3		
No	85	770.6±68.1		
Nocturnal symptoms			0.12	-788.1 – 98.1
Yes	49	1244.3±212.4		
No	134	899.3±61.8		
Self-reported burden of asthma			0.01	-667.7 – -88.9
No	94	807.7±68.9		
Yes (mild – severe)	89	1186.0±129.0		
Exposure to indoor smoke			0.87	-368.6 – 314.6
Yes	43	1012.3±213.0		
No	140	985.3±70.4		
Influenza vaccination			0.07	-24.9 – 498.0
Yes	68	843.0±79.5		
No	115	1079.6±106.0		
Current use of short-acting ß2 agonist			<0.01	-683.6 - -211.7
Yes	135	1109.1±93.7		
No	48	661.4±74.0		
Current use of preventive drugs			<0.01	-791.6 – -326.6
Yes	128	1159.7±97.1		
No	55	600.6±66.7		
Disease severity			<0.01	-1197.2 - -463.7
Intermittent	124	723.9±54.6		
Persistent	59	1554.4±175.5		
Current use of emergency service and/or hospitalization			<0.01	-1115.9 - -236.7
No	137	821.7±61.8		
Yes	46	1498.0±210.2		

Table IV. Types of Costs Acording to Disease Severity

	Intermittent asthma		Persistent asthma			
	Mean±SEM	%Total	Mean±SEM	%Total	P	CI
Outpatient	357.0±28.5	49.3	743.3±111.5	47.8	<0.01	-616.2 – -156.2
Emergency*	106.0±14.4	2.7	132.5±18.0	3.0	<0.01	-50.2 - -4.8
Hospitalization**	1395.6±702.3	3.1	808.8±142.1	5.2	>0.05	-137.3 – 17.8
Medication ***	141.1±16.1	19.4	307.6±45.3	19.7	<0.01	-262.4 - -70.6
Total	723.9±54.6	100.0	1554.4±175.5	100.0	<0.01	-1197.2 - -463.7

* The descriptive statistics of emergency costs of the patients who admitted to emergency services within the previous 1 year (n=44).

** The descriptive statistics of hospitalization costs of the patients hospitalized within the previous 1 year (n=8).

*** Total annual costs of short-acting ß2 agonists, preventive drugs, and nasal, oral and i.v. corticosteroids and antihistamines.

to the univariate analysis, gender, another allergic disease, asthmatic mother, being atopic, nocturnal symptoms, exposure to indoor smoke, influenza vaccination, hospitalization, use of emergency care and parental education were not predictive of total cost of asthma, whereas age, composite index for current use of emergency care and/or hospitalization, current use of preventive drugs, exercise-induced symptoms, self-reported burden of asthma, current use of short-acting ß2 agonists and disease severity were predictive of total costs. Patients aged between 3-11 years had higher costs than patients aged 12 and older (mean difference=US$315.5±127.2, p<0.05). Furthermore, the costs of preventive drugs (ICS, LTRA and beta-2/ICS combination) were more prominent for persistent asthmatics (mean difference=US$134.8±42.7, p<0.01). Outpatient, emergency and medications costs of persistent asthmatics were higher than those of intermittent asthmatics. Furthermore, persistent asthmatics had higher total direct costs per patient than intermittent asthmatics (mean difference= US$676.3±219.1, p<0.01).

As shown in Table V, the multivariate analysis indicated that the determinants of direct costs of childhood asthma were disease severity, current use of preventive drugs and current use of emergency sevice and/or current hospitalization. Current use of preventive drugs, having a current use of emergency service and/or current hospitalization and having persistent asthma were found to increase the costs by 3.1 (p<0.01, CI=1.4-6.5), 2.6 (p<0.02, CI=1.2-6.0) and 4.3 (p<0.01, CI=2.0-9.2) times, respectively.

Discussion

This unique study attempted to investigate for the first time the cost of pediatric asthma in Turkey and showed that the mean total annual cost of pediatric asthma is almost US$1,000, which accounts for 12% of the yearly income of a family. The majority of the yearly cost comes from outpatient costs (48.5%); any hospitalization causes an additional cost nearly equal to the yearly cost (US$955.5±16.5). The predictors of costs of childhood asthma appeared to be disease severity, current use

Table V. Binary Logistic Regression Analysis of Total Direct Costs of Childhood Asthma

Model	OR	P	CI
Disease severity			
Intermittent	1.0(Ref)		
Persitent	4.3	<0.01	2.0-9.2
Current use of any preventive drug			
No	1.0(Ref)		
Yes	3.1	<0.01	1.4-6.5
Current use of emergency service and/or current hospitalization			
No	1.0(Ref)		
Yes	2.6	<0.02	1.2-6.0

Model: Adjusted for age, presence of asthmatic mother, nocturnal symptoms, comorbid allergic disease, self-reported burden of asthma and influenza vaccination.

of preventive drug and having current use of emergency care and/or current hospitalization. These findings provide insights into the cost of pediatric asthma and may hopefully direct policy decisions towards a better management of the disease.

According to our current understanding, the rate of asthma increases as communities adapt to western lifestyles. Worlwide, the prevalence of pediatric asthma differs between countries from 1.5% to 20.0%. Particularly, in western countries such as the United Kingdom, the United States and Australia, the prevalence of childhood asthma reaches 20%[12,14], whereas in Asian countries it varies between 1.5% and 6.2%[3]. Turkey has an asthma prevalence of 7.0% in schoolchildren[21]. As one of the most common chronic diseases in childhood, asthma causes an important economic burden for families, the health system and the community. Knowledge of its magnitude and determinants is critical for development of management strategies. The economic evaluation of the disease can provide insights into how health care resources are distributed and can lay the basis for further policy decisions[22]. In the studies conducted in Canada and the United States, it has been shown that the mean total direct costs were US$504 and US$2697 per year, respectively, suggesting a large variation in asthma-related cost values between countries due to the differences in the treatment of the disease, unit cost values of expenditures at inpatient and outpatient care facilities, and the items constituting the indirect cost. The mean annual cost achieved in this study is somehow between these two, at a value of US$991.7±73.2. In a recent trial, mean annual direct medical costs of adult asthma was demostrated to be US$1,465.7±111.8 per capita in Turkey[23], suggesting more significant economical burden of asthma in adults compared to children. However, further comparative trials are required to delineate a definitive conclusion for the difference between age groups.

Besides preventing asthma-related deaths, reducing the number of asthma-related hospitalizations and emergency care requirements are well-established primary goals of asthma guidelines. Expenses of hospitalization and emergency care comprise the major fraction of asthma-related cost in many countries[5,15,18]. In our study population, current hospitalization was not predictive of the cost of asthma nor was current use of emergency care. There are a number of potential reasons for this lack of association. However, by using a composite index for both hospitalization and emergency care, we demonstrated that they predict the cost of the disease. During recent decades, through effective use of preventive (anti-inflammatory) drugs in persistent asthma, hospitalization rates seemed to have decreased due to adequate control of the disease[9,10]. For instance, hospitalization rates for asthmatics in the United States declined from 16% to 8% between 1980 and 1994. The hospitalization rate was 22% in a study conducted in Brazil, Mexico and Argentina[2]. In our study group, the hospitalization rate was 4.4% for the recent year and we believe that this low rate explains why hospitalization alone does not predict the cost. Although emergency care use was frequent (24.4%), it was also not predictive of the cost and a potential reason may be the low cost of emergency visits. One of the most probable reasons for frequent emergency care use is the ease of using emergency care in our country; there is also a common sense in the use of emergency service instead of an unscheduled visit. As a consequence, by using a composite index for both of hospitalization and emergency care, we demonstrated that they predict the cost of the disease and that both reflect inadequately controlled disease. In recent years, medication costs have emerged as the largest component of the direct cost of asthma. In line with the declining trend in hospitalizations, the proportion of hospitalization costs to total direct medical costs also declined. In our study population, hospitalization costs were 4.2% of total direct costs. These values are lower than previous findings of 15%, 20.5% and 13.1% in the United States, Canada and Australia, respectively[5,13,18].

There are clearly some limitations to this study and the results obtained therein. First, our clinic is a referral university center and functions as a tertiary allergy clinic as documented by the frequent use of laboratory settings. The outpatient visits have a cost comparable to that of emergency visits because of the frequent use of laboratories, such as for lung function and skin tests, which may lead to an increased cost of asthma. However, the low rate of current hospitalization reduces

the cost of asthma, and we believe that the better quality of the health care, as evidenced by reduced hospitalizations, might at least balance the increased costs of outpatient visits to the tertiary health service. The documented cost of asthma, though it does not reflect the current status in the country, provides the first objective data regarding potential costs. Because of the potential for lower quality of health care in rural areas, a higher cost may be expected for the whole country. Another potential bias in the study arises because of adjustments we made for some cost data. As was indicated previously, some of the costs were unavailable and were therefore extrapolated from the mean costs of available data. This increases the likelihood that the prices and the costs of our clinic significantly affected the total cost. Our center is a reference clinic and the costs of laboratory examinations might be more expensive than in other health care facilities in the country.

There have been two types of studies investigating the economic burden of asthma: population-based sampling frames which provide estimates for nations and entire regions, and studies like ours using clinical-based sampling frames[5,24]. Each study environment has its own intrinsic strengths and limitations[1,7]. The clinical- based studies of cost of childhood asthma have more diagnostic certainty on disease severity, which has a great impact on the cost of asthma[1,5,25]. One of the limitations of our study was the lack of indirect costs. We did not assign a monetary value to lost work days and lost productivity of the parents/caregivers. In Turkey, workers do not forfeit their daily income when they cannot go to work in spite of loss in national production. In our study as well, none of the parents/caregivers loss their daily income. Employers are quite tolerant towards their employees who are unable to work due to their children's illnesses. Thus, traditional behavior trends may affect the costs of asthma, as observed in Turkey.

In multivariate analysis, we documented that disease severity and use of preventive drugs were two other predictive factors for the cost of asthma in our study population. Medication cost constituted almost 15% of total cost of asthma and this figure is similar to previous studies, which have reported that drug costs account for 6.1–22.3% and 50% of the total direct cost of asthma, respectively[5,18]. A reasonable explanation for this relationship could be the higher prices of the newer asthma drugs such as long-acting inhaled ß2-agonists and leukotriene modifiers compared with the previously used theophylline and inhaled corticosteroids. The adequate control of the disease plays the key role in decreasing the total direct costs, although it increases the costs of medication and outpatient visits. Our findings also denote that the overall cost of asthma was correlated with the severity of asthma. Though persistent asthma patients constituted the minority of the study group, its total annual cost was two-fold that of intermittent asthmatics. These findings are in line with literature data, and as expected, total cost of asthma and cost of preventive drugs increase with increasing severity. Furthermore, these findings may suggest that intervention strategies targeting persistent asthma patients are required to decrease the cost of the disease.

Although asthma care in most patients should be performed in the primary care settings by local physicians, the majority of our patients (56.8%) came from other cities of the country, which contributed transportation costs of 8.8% of the total costs for the study group. In Turkey, perception among the general population is that asthma is an unfavorable disease which may lead to severe disablement. As a result, parents tend to prefer to treat their children in the most experienced clinics. As a consequence, most of our patients are intermittent patients, and this causes additional costs like transportation and hotel costs. Although use of alternative/complementary therapies is popular in Turkey and in our study population, the contribution of this type of cost per patient was low, at 2.1%. In a previous study, we have shown that the major predictors for the use of alternative/complementary therapies are low asthma control, i.e. unmet expectations; advise of relatives and friends are the major source of this worldwide trend[26-29].

In conclusion, this study provides valuable information about the determinants of the direct costs of childhood asthma and may serve as a baseline for further studies and trends over time. The outpatient and medication costs were predominant among the direct costs of childhood asthma in the study population. Adequate

disease control plays a key role in decreasing the total direct costs, although it increases the medication and outpatient costs.

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