

Direct Medical Cost of Asthma in Ankara, Turkey

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Key Words

Asthma · Medical cost, direct

Abstract

Background: There has been no documented data regarding the cost of asthma in our country. **Objective:** In this 1-year prospective study, we aimed to determine the annual cost of asthma in Ankara, Turkey. **Methods:** Direct medical cost analysis was performed in 118 patients. **Results:** Mean annual direct medical costs of asthma were USD 1,465.7 ± 111.8 per capita. Medication cost comprised the majority (81%) of the total direct cost. Mean direct medical costs according to the stage of disease were USD 172.5 ± 51.7, 860.7 ± 70.2, 1,671.6 ± 141.8 and 3,491.9 ± 417.6 for stage 1 (n = 4), 2 (n = 54), 3 (n = 46) and 4 (n = 14) patients, respectively. **Conclusions:** In this first study to document the cost of asthma for our region, direct cost of asthma was found to be increased with the severity of the illness. Considering the fact that medication cost comprises the major fraction of the direct cost, cost-effectiveness trials to determine the effective treatment with optimal cost for different asthma stages should be the next step.

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Introduction

Asthma has emerged as a major public health problem and has been estimated to affect 1.3 million adults in Turkey with a mean prevalence of 5% [1, 2]. Recent trials demonstrated an increase in prevalence of the disease worldwide [3, 4]. Parallel to the increase in the morbidity of asthma, an increase in the cost of the disease has also been reported [5, 6]. Hence, the economic burden of asthma is a current topic of interest in many countries. 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 that can direct financial resources more effectively toward the management of the disease. In the USA, the cost associated with asthma represented 1% of total healthcare costs in 1990 [7]. However, there is a large variation in asthma-related cost values amongst different 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 [8]. As a major factor, a higher degree of disease severity has been suggested to increase the total cost of asthma [9, 10].

In a recent trial, we demonstrated that most asthma patients had mild disease severity and severe asthma could only be found in 7% of the subjects [11]. However,

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there is no data about the economic burden of asthma and the influence of varying degrees of severity on the cost of disease in our country. In this 1-year prospective study, we aimed to determine the annual cost of asthma per capita and to evaluate the relationship between the disease severity and the cost of asthma in patients treated according to the Global Initiative for Asthma (GINA) [12] and national asthma [13] guidelines.

Material and Methods

Patients

The study was prospectively carried out in our tertiary care clinic located in Ankara, the capital city of Turkey. Between December 2000 and June 2001, asthma patients admitted to our outpatient clinic were consecutively enrolled in the study. The study population included patients from both Ankara and various other regions of Turkey. Participants included residents of both inner city and small towns. The diagnosis of asthma was based on a history of recurrent

symptoms of wheezing, shortness of breath, cough and demonstration of objective signs of reversible airway obstruction by means of at least >12% increase in FEV₁ after 15 min with an inhalation of 200 µg salbutamol [12–14]. Exclusion criteria were chronic obstructive pulmonary disease indistinguishable from asthma, instable asthma for the preceding 4 weeks requiring a change in asthma treatment and/or medical care due to acute exacerbation of symptoms.

Study Design

Initial Evaluation

Severity Assessment. At the beginning of the study, asthma severity was determined by allergy and chest disease specialists on the basis of the frequency of asthma symptoms, pulmonary function tests, and medication requirements according to the international/national guidelines [12, 13] for chest disease, and was classified as stage 1 = intermittent, stage 2 = mild persistent, stage 3 = moderate persistent and stage 4 = severe persistent asthma.

Atopy Evaluation. The atopic status of the asthmatic subjects was evaluated according to skin prick tests (SPTs) and/or specific IgE results. SPTs were performed with a standardized panel including *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, grass, tree, weed pollens, cat, dog, cockroach, alternaria and cladosporium

Table 1. Unit costs of procedures and most commonly used drugs for asthma and rhinitis

	Cost (USD)		Cost (USD)
a Procedure			
Physician visit (outpatient service)	7.4	Specific IgE (per allergen)	32.1
Pulmonary function test	30.5	Differential blood count	35.5
Methacholine provocation test	42.7	Blood biochemistry	35.5
SPT (per allergen)	6.1	Injection	1.7
Chest X ray	13.5	Treatment with nebulizers	6.6
Sinus X ray	10.1	Nasal oxygen treatment (per hour)	1.2
Blood gas analysis	17.0	Hospital stay (per day)	11.1
b Medications			
Beclaforte inhaler ^a	66.0	Foradil [®] inhaler ^h	147.6
Becodisc ^{®a}	33.4	Foradil [®] aerolizer ^h	87.2
Flixotide [®] inhaler 125 µg ^b	44.0	Oxis [®] turbohaler 9 µg ^h	68.6
Flixotide [®] discus 250 µg ^b	88.8	Serevent [®] inhaler ⁱ	56.4
Pulmicort [®] turbohaler 100 µg ^c	45.6	Serevent [®] discus ⁱ	115.5
Pulmicort [®] turbohaler 200 µg ^c	45.6	Rhinocort [®] aqua nasal spray ^j	36.3
Pulmicort [®] turbohaler 400 µg ^c	86.9	Flixonase [®] nasal spray ^k	45.8
Miflonide [®] 200 µg ^c	29.4	Nasonex [®] nasal spray ^l	46.6
Miflonide [®] 400 µg ^c	59.1	Zyrtec [®] tablets ^m	14.5
Ventolin [®] inhaler ^d	9.3	Claratine [®] tablets ⁿ	17.8
Bricanyl [®] turbohaler ^e	27.8	Telfast [®] tablets ^o	22.8
Singulair [®] 10-mg tablets ^f	95.9	Allerset [®] tablets ^m	5.8
Accolate [®] 20-mg tablets ^g	95.7	Xanthium [®] capsule ^p	9.8

^a Beclamethasone DP; ^b fluticasone DP; ^c budesonide; ^d salbutamol; ^e terbutaline; ^f montelukast; ^g zafirlucast; ^h formoterol; ⁱ salmeterol; ^j budesonide; ^k fluticasone DP; ^l mometasone furaoate; ^m cetirizine; ⁿ loratadine; ^o fexofenadine; ^p theophylline.

antigens (Stallergenes, France). Specific IgE was measured by the Pharmacia CAP system according to the manufacturer's instructions (Pharmacia, Uppsala, Sweden). Results equal to or greater than class II (IgE level ≥ 0.7 kU/l) were considered positive.

Comorbid Disorders. Subjects were also evaluated for the presence of comorbid diseases associated with asthma such as chronic rhinosinusitis, allergic rhinitis, nasal polyps and analgesic intolerance.

After having entered the study, patients were followed for 1 year. At every visit, they were evaluated by allergy and chest disease specialists. The treatment and visit programs suggested for the patients were not violated and patients continued with their ongoing treatment schedules arranged according to the guidelines [12, 13]. In case of a failure of the treatment, the patient was reevaluated and the treatment and visit programs were rearranged.

Evaluation of the Cost

Direct medical cost of the disease was evaluated at the end of a 1-year follow-up period for each patient. Cost was expressed in US dollars using the purchasing power parity (PPP) value of Turkey in 2002.

Direct medical cost included the costs of the visits of the physicians, diagnostic tests, emergency room and other health care services, medications and hospitalizations. The cost of visits included the physicians' visits. Diagnostic tests included the tests directly related to asthma such as pulmonary function tests, methacholine provocation tests, reversibility tests, chest X ray, sinus X ray, SPTs, determination of specific IgE levels, consultations and other tests (table 1). The cost of emergency room or other health care services included examination fee, consultations, medications and other medical care performed in the emergency room or other health care services. Hospitalization cost included the cost of the bed, medical procedures, medications, consultations and medical supplies provided during the period of hospitalization.

For inpatient and outpatient services, the unit price lists, provided by the accounting department of the Ankara University Hospital, were used. Within a prospective design, the use of resources was recorded at each visit and at the end of 1 year; the frequency of the use of resources for each item was determined from the hospital case records for each patient.

Medication cost included the cost of drugs prescribed for asthma such as bronchodilators, inhaled corticosteroids, leukotriene modifiers, antibiotics and other drugs including theophylline, cromones, mucolytics and oral steroids. Prescription cost of comorbid upper airway diseases was calculated according to prescription of nasal corticosteroids, antihistamines, antibiotics, and nasal decongestants. At the end of 1 year, the total number of boxes used was determined on the basis of the case record of each patient. Unit cost of medications was based on pharmaceutical market prices that were determined by the Ministry of Health of Turkey for the year 2002.

Total direct cost per capita was calculated by the equation of 'total cost = unit cost \times resource use' for each resource item including the costs of physician visits, diagnostic tests, emergency room and other health care services, medications and hospitalization.

Statistical Analysis

Numeric values were expressed as mean \pm SEM. Ordinal values were expressed as number (percentage). Owing to the nonhomogeneous distribution of the study parameters among groups, nonparametric tests were chosen for the overall statistical analysis. Intergroup comparisons of numeric values were accomplished by the Kruskal-

Table 2. Demographic and disease features of the study group

Patient number	118
Sex distribution	
Female/male	91/27 (77.1/22.9)
Age, years	41.6 \pm 1.0
Occupation	
Housewife	61 (51.7)
Student	5 (4.2)
Officer	38 (32.2)
Retired	14 (11.9)
Education	
Primary school	42 (35.6)
High school	23 (19.5)
University	35 (29.7)
Current smokers	6 (5.1)
Atopy rate	47 (39.8)
Comorbid disorders	
Allergic rhinitis	26 (22.0)
Sinusitis	69 (58.5)
Nasal polyps	23 (19.5)
Analgesic intolerance	20 (16.5)
Asthma severity	
Intermittent (stage 1)	4 (3.3)
Mild persistent (stage 2)	54 (45.8)
Moderate persistent (stage 3)	46 (38.9)
Severe persistent (stage 4)	14 (11.9)
Disease duration, years	9.2 \pm 0.7
Initial FEV ₁ , l/s	2.6 \pm 0.1 (88.2 \pm 2.2)
Final FEV ₁ , l/s	2.7 \pm 0.9 (92.8 \pm 2.1)

Values in parentheses represent percentage.

Wallis analysis of variance method. In case of a significant result after the Kruskal-Wallis test, post hoc Mann-Whitney U tests with p values adjusted downward to 0.008 (0.05 divided by 6, the number of pairwise comparisons in 4 groups) were performed. For within-group comparisons of numeric variables, a Wilcoxon matched-pair test was used. For comparison of ratios, χ^2 test was performed. All p values were bidirectional and values less than 0.05 were considered as statistically significant. The Statistical Package for Social Sciences (SPSS) for Windows v10.0 was used for the analysis.

Results

Patients

Of 145 asthmatic patients enrolled in the study, 118 completed the study protocol (table 2). The remaining 27 subjects who were not able to complete the follow-up vis-

Table 3. Demographic and disease features according to severity groups

	Stage 1 (n = 4)	Stage 2 (n = 54)	Stage 3 (n = 46)	Stage 4 (n = 14)	p ^a
Sex distribution					
Female	2 (50)	44 (81.5)	37 (80.4)	8 (57.1)	0.02
Male	2 (50)	10 (18.5)	9 (19.6)	6 (42.9)	
Age, years	37.5 ± 6.0	38.5 ± 1.3	43.9 ± 1.6	47.5 ± 3.6	0.003
Asthma duration, years	7.0 ± 1.2	7.0 ± 0.8	9.9 ± 1.2	15.7 ± 2.0	0.002
Current smokers	0 (0)	2 (3.7)	4 (8.7)	0 (0)	NS
Atopy rate	2 (50)	25 (46.3)	19 (41.3)	1 (7.1)	<0.0001

Figures in parentheses represent percentage. NS = Nonsignificant.

^a Kruskal-Wallis test among different severity groups.

Table 4. Annual frequency of use of resource items in the study group

Procedures	
Physician visit (outpatient service)	3.6 ± 0.1
Pulmonary function test	3.3 ± 0.1
Methacholine provocation test	1.1 ± 0.1
SPTs (per allergen)	22.6 ± 0.5
Chest X ray	1.0 ± 0.0
Sinus X ray	1.0 ± 0.0
Blood gas analysis	1.0 ± 0.0
Specific IgE (per allergen)	3.8 ± 1.4
Differential blood count	1.1 ± 0.1
Blood biochemistry	1.1 ± 0.0
Emergency room visit	1.4 ± 0.2
Injection	1.5 ± 0.2
Treatment with nebulizers	1.2 ± 0.2
Nasal oxygen treatment (hours)	4.0 ± 2.0
Hospital stay (days)	35.3 ± 8.7

Values are expressed as mean ± SEM.

its were subsequently excluded. The distribution of sex (female/male: 24/3), age (39.5 ± 1.3 years), disease duration (12.3 ± 1.4 years) and severity [stage 1 = 0 (0%), stage 2 = 14 (51.9%), stage 3 = 9 (33.3%), stage 4 = 4 subjects (14.8%)] in patients who were lost to follow-up were similar compared with the eligible study population (table 2).

Distribution of Asthma Severity

There were 4 (3.4%), 54 (45.8%), 46 (39%) and 14 subjects (11.9%) in stage 1, 2, 3 and 4 asthma severity, respectively. Mean age and mean duration of asthma, which

were increasing with the severity of the disease, were significantly different between groups ($p = 0.029$ and $p = 0.002$, respectively) (table 3). The rate of atopy was lower in severe asthmatics ($p < 0.0001$).

Direct Cost Evaluation

The frequency of the use of resource items is given in table 4. Mean annual direct cost of asthma was calculated as USD 1,465.7 ± 111.8 per capita for 1 year (table 5). Mean prescription cost of USD 1,188.0 ± 93.0 accounted for the majority (81%) of the total direct cost.

Distribution of Cost according to Severity of Asthma

Mean direct medical costs of USD 172.5 ± 51.7, 860.7 ± 70.2, 1,671.6 ± 141.8 and 3,491.9 ± 417.6 in the groups at stage 1, 2, 3 and 4, respectively, were significantly different ($p < 0.0001$) and exhibited a trend towards an increase with the severity of disease (table 5). The mean cost of physician visits and number/cost of pulmonary function tests also increased with the disease severity ($p = 0.035$ and $p = 0.007$, respectively). Mean medication cost was also found to be higher in severe asthma ($p < 0.0001$). The cost of emergency room and other health care services was similar ($p > 0.05$).

Medications accounted for the majority of the cost in stage 2, 3 and 4 asthma patients comprising 75, 85.3 and 81.1% of the direct costs, respectively. Medication costs according to the severity of the illness are summarized in table 6. Long-acting inhaled β_2 -agonists and inhaled corticosteroids predominated at all stages except stage 1. Mean use/cost of inhaled steroids and long-acting inhaled β_2 -agonists increased with the degree of asthma severity ($p < 0.0001$). There was no difference in nasal medication cost between different asthma stages ($p > 0.05$).

Table 5. Total direct cost of asthma in the whole study group and in different severity groups

	Whole group (n = 118)	Stage 1 (n = 4)	Stage 2 (n = 54)	Stage 3 (n = 46)	Stage 4 (n = 14)	p ^a
Physician visits	26.8±0.8	16.7±1.9	25.4±1.3	28.1±1.6	29.9±2.4	0.035
Diagnostic tests	191.3±12.2	130.9±49.8	184.2±18.8	213.1±21.5	160.6±12.5	NS
Medications	1,188.0±93.0	20.1±10.9	645.5±67.3	1,425.4±132.0	2,833.4±216.2	<0.0001
Emergency room/other health care services	4.8±1.6	4.2±4.2	5.0±2.7	4.5±3.2	3.4±3.4	NS
Hospitalization	54.9±32.9	0.0±0.0	0.0±0.0	0.0±0.0	464.3±261.3	<0.0001
Total cost	1,465.7±111.8	172.5±51.7	860.7±70.2	1,671.6±141.8	3,491.9±417.6	<0.0001

Values are given as mean ± SEM US dollars. NS = Not significant.

^a Kruskal-Wallis test among different severity groups.

Table 6. Medication costs in different severity groups

	Stage 1	Stage 2	Stage 3	Stage 4	p ^a
Inhaled steroids	10.9±10.9	437.0±48.2	781.7±72.1	1,660.2±18.5	<0.0001
Long-acting inhaled β ₂ -agonists	0.0±0.0	106.0±27.3	539.8±83.4	1,108.2±85.6	<0.0001
Short-acting inhaled β ₂ -agonists	9.3±0.0	14.8±1.6	19.9±3.2	21.7±3.9	NS
Leukotriene modifier	0.0±0.0	65.7±44.8	64.6±34.4	0.0±0.0	<0.0001
Oral steroids	0.0±0.0	0.8±0.8	1.8±1.3	12.2±9.3	<0.0001
Antibiotics	0.0±0.0	20.1±7.1	17.2±7.7	20.7±11.9	<0.0001
Other asthma medications	0.0±0.0	1.1±1.1	0.008±0.0	10.3±5.3	<0.0001
Total medication cost	20.1±10.9	645.5±67.3	1,425.4±131.9	2,833.4±216.2	<0.0001

Values are given as mean ± SEM US dollars. NS = Not significant.

^a Kruskal-Wallis test among different severity groups.

Cost of Prescription for Rhinitis

Allergic rhinitis, chronic sinusitis and nasal polyps were observed in 26, 69 and 23 subjects, respectively. Mean medication cost per capita was USD 178.3 ± 49.5 for allergic rhinitis, 157.1 ± 25.7 for chronic rhinosinusitis and 268.2 ± 59.1 for nasal polyps.

Discussion

In this study, we established annual direct medical costs of asthma per patient as USD 1,465.7 when managed according to the guidelines in a tertiary clinic. In the USA, the total cost of asthma was estimated as USD 5.8 billion, 6.2 billion and 12.7 billion in 1987, 1990 and 1998, respectively [7, 15]. Asthma-related total cost in developed countries has been reported to range between

USD 326 and 1,315 per patient [7, 8, 16, 17]. In Switzerland and in Spain, annual asthma-associated costs have been found to amount to CHF 1,200 million and € 900–1,200 million, respectively [18, 19]. Taking the midyear population count of 67 million into account, the number of adults with asthma would be about 1.3 million in our country. Based on the mean direct medical costs of asthma of USD 1,465.7 per person demonstrated in our study, the direct cost of asthma in Turkey could be estimated to be around USD 1.9 billion for 1 year. Although there is a similarity to international figures, a reliable comparison for asthma-associated cost among different countries might be quite difficult because of the differences in the unit cost, study periods, exchange rates and annual inflation rates. PPP is a theory stating that exchange rates between currencies are in equilibrium when their purchasing power is the same in two countries. The basis of

PPP is the 'law of one price' and taking annual inflation rates into consideration provides superiority of PPP in comparison with exchange rates [20]. In our study, cost calculations were expressed in US dollars using the PPP value of Turkey in 2002.

Previous studies reported that hospitalization expenses comprised the major fraction of asthma-related cost in many countries [15]. However, following the use of anti-inflammatory drugs in persistent asthma patients, hospitalization rates seemed to have decreased due to adequate control of the disease [9, 10]. Now, medication costs have replaced the hospital costs as the largest component of the direct cost of asthma. Except in the elderly, the total asthma cost was reported to be higher than adult asthmatics due to a greater use of medications as well as frequent and longer hospital stays in this particular group [21].

Medication cost constituted the majority (81%) of total medical expenditures in our study. This figure is higher than in previous studies which report that drug costs make up 30–40% of the total direct cost of asthma [7, 9, 10, 19]. A reasonable explanation for this discrepancy could be the higher prices of newer asthma drugs such as inhaled corticosteroids, long-acting inhaled β_2 -agonists and leukotriene modifiers compared with the previously used oral theophylline, and inhaled cromones or it might be also due to lower unit cost of diagnostic tests and physician visits in our country compared with the international figures (table 1).

The increase in the cost of asthma is reported to be mainly due to uncontrolled severe disease [22]. In a study by Van Ganse et al. [23], medical resource utilization per capita was € 549.8 for well-controlled patients and € 1,451.3 for patients with poor control. Similar to this finding, Herjavec et al. [24] showed that asthma cost increased with uncontrolled disease. In a recent trial, we have shown that patients with severe asthma had more hospitalizations for asthma attacks [25]. Our current findings denoted that the overall cost of asthma was correlated with the severity of asthma. Severe asthma patients constituted the minority of the study group but its direct cost was 2-fold, 4-fold and 20-fold higher compared with moderate-persistent, mild-persistent and intermittent asthma, respectively. Hospitalization cost made up a substantial increase in the total medical cost of severe disease with a 13.3% contribution to the total expenditure. These findings might suggest that intervention strategies targeting severe asthma patients could decrease the cost of the disease in our population.

As is true of any study, there are limitations in the economic analysis of the diseases and one must be cautious in the interpretation of the results. In the current study, every attempt was made to address the major components of the cost of care and it was not possible to estimate some asthma-related expenditures such as the cost of patient education, the use of nebulizer therapy at home in severe asthmatics, telephone calls, and others. Though encountered in less than 10% of patients, another problem was the reliability of other health care expenditures such as emergency room service and primary care physician admissions at centers other than our clinic. This information, primarily depending on the patients' information, is subject to a potential recall bias which should be kept in mind in the cost analysis.

Contrary to a trend towards an increment in the cost of resource items with advanced health care services in most western countries, the unit prices of resource items of a university hospital are identical to secondary care hospitals in Turkey. Moreover, the prices of the medications are constant throughout the country owing to the policy of the Ministry of Health. In primary care, the charge of outpatient visits is half of that in secondary and tertiary care clinics, but there is no inpatient facility and many of the resources required for the diagnosis and follow-up of asthma are not available in the primary care health services. The results of the current study reflect the cost of asthma of patients followed in a tertiary care clinic but might also be reproducible for other health care steps in our country except some minor changes in the primary care.

In many countries, cost analysis of asthma is retrospective and based on the data of national health statistics. However, in our study, data collection was prospective and treatment and management strategies were arranged according to international/national asthma guidelines which have previously been known to decrease asthma cost by controlling symptoms well [26, 27].

In conclusion, this is the first study to document the direct medical cost of asthma in our region. As severe asthma is demonstrated to have a higher hospitalization rate, require an augmented number of medications and constitute the major cost of the illness, these patients require particular interventional strategies such as intensive education of both patients and physicians and also a close follow-up in a tertiary care clinic in order to decrease morbidity as well as the cost of the disease. Based on the fact that the medication cost is the major contributor of the direct cost, effective treatment with optimal cost for the different stages of asthma severity remains to be delineated by further cost-effectiveness trials.

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