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Economic burden of severe asthma in Turkey: a cost of illness study from payer perspective

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Key words

Severe asthma; asthma attack; practice patterns; direct costs; cost analysis; Turkey.

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Doi
10.23822/EurAnnACI.1764-1489.149

Summary

Objective. *To estimate economic burden of severe asthma in Turkey from payer perspective based on expert panel opinion on practice patterns in clinical practice.* ***Methods.*** *This cost of illness study was based on identification of per patient annual direct medical costs for the management of severe asthma in Turkey from payer perspective. Average per patient direct medical cost was calculated based on cost items related to outpatient visits, laboratory and radiological tests, hospitalizations and interventions, drug treatment and equipment, and co-morbidities/complications.* ***Results.*** *Based on total annual per patient costs calculated for outpatient admission ($ 177.91), laboratory and radiological tests ($ 82.32), hospitalizations/interventions ($ 1,154.55), drug treatment/equipment ($ 2,289.63) and co-morbidities ($ 665.39) cost items, total per patient annual direct medical cost related to management of severe asthma was calculated to be $ 4,369.76 from payer perspective. Drug treatment/equipment (52.4%) was the main cost driver in the management of severe asthma in Turkey, as followed by hospitalizations/interventions (26.4%) and co-morbidities (15.2%).* ***Conclusions.*** *In conclusion, our findings indicate that managing patients with severe asthma pose a considerable burden to health economics in Turkey, with medications as the main cost driver.*

Introduction

Asthma is a chronic disease with a high prevalence (4.3%) in adults and is a global health, social and economic problem affecting 300 million individuals worldwide (1-3). The prevalence of asthma in Turkey was documented to be 7.4% in Global Initiative for Asthma (GINA) - Global Burden of Asthma Report (4), while approximately 3-4 million people in Turkey have been considered to suffer from asthma (5). Asthma has been associated with significant economic burden in terms of both direct and indirect costs leading to considerable increase in medical expenditures and productivity loss in conjunction with the high prevalence of the disease (6, 7).

Severe asthma was defined by World Health Organization in 2009 as "uncontrolled asthma which can result in risk of frequent severe exacerbations (or death) and/or adverse reactions to medications and/or chronic morbidity" and categorized into 3 groups including untreated severe asthma, difficult-to-treat severe asthma, and treatment-resistant severe asthma (8). Accordingly, while patients with severe asthma comprise only 5% to 10% of overall asthmatic population (9-11), severe asthma was associated with use of almost 80% of health resources allocated to the disease and considered to be responsible for 50% of all direct and indirect healthcare costs (12-18).

Both asthma severity and presence of asthma exacerbations are considered amongst the important risk factors for increased asth-

ma cost (6, 12, 13, 16, 19, 20), particularly in terms of increased health care utilization and costs due to increased hospitalizations (20-22). Considerable percentage of patients with severe asthma have a poor therapeutic response to available pharmacotherapy and continue to experience exacerbations despite the use of intensive therapy (15, 18, 23-25). This seems notable given the almost 2-fold cost increment in asthma-related costs among patients with severe asthma who experience exacerbations compared to patients with controlled severe disease (25, 26).

In past studies on economic burden of managing asthma, higher average annual direct costs were reported in patients with persistent asthma as compared with non-asthmatic control subjects (27), in severe persistent asthma as compared with mild and moderate persistent asthma (6, 14, 28, 29), in poorly controlled asthma as compared with controlled asthma (21, 26, 30), and in patients with than without exacerbation (6, 21, 25, 31), while limited data are available on the impact of acute asthma exacerbations in severe asthma patients (20, 25, 31).

Asthma exacerbation has a high prevalence in Turkey which results in increased hospital costs, long-term treatment and complications and thus further cost increment. While the treatment is reimbursed totally by the Turkish healthcare system, in a monopsony market based on government reimbursement and overall coverage of health insurance for the entire population, treatment costs for diseases necessitating long-term and expensive treatments often extends the amount of reimbursement, particularly in tertiary care hospitals. In fact, expert panel-based cost-of-illness studies have recently become popular in literature despite they are an established consensus-finding method in clinical and health services research considered very important in terms of public health investigations and health strategy development. Given the cost increment associated with uncontrolled disease status and ongoing restrictions in the healthcare budgets, this type of data should be more extensively addressed by researchers and be discussed on appropriate platforms to enable awareness raising and more efficient use of healthcare resources.

This cost of illness study was therefore designed to determine economic burden of severe asthma in Turkey from payer perspective and in relation to acute attack and attack-free periods.

Methods

Design

This cost of illness study was based on identification of per patient annual direct medical costs for the management of severe asthma in Turkey based on expert panel opinion on practice patterns in clinical practice. Direct medical cost was calculated based on cost items related to outpatient visits, laboratory and radiological tests, hospitalizations/interventions, drug treatment/equipment and co-morbidities.

Data on real life clinical practice

Data on real-life practice patterns in the management of severe asthma in Turkey including outpatient clinic admission rates, laboratory and radiological investigations, selected medications, hospitalizations and interventions were based on expert panel consensus. Expert panel members were from selected from 14 tertiary healthcare centers for Pulmonology and Allergy and Immunology diseases providing severe asthma patient care across Turkey, by the Project Advisory Board of the study according to the geographical distribution of specialists in Turkey. The participating 17 experts (professors, also international speakers and national influencers), who had at least 15 years of experience in Pulmonology and Allergy and Immunology were invited to participate in the meeting and informed about the study via e-mail and asked to fill a standardized form reflecting data from their clinic before attending the meeting. Hence each expert participated in the consecutive meetings to achieve the proposed consensus based on data provided for different clinics reflecting actual patient data used to fill out the forms, based on sampling of overall 20,879 patient admissions per year. The panel critically analyzed the previously published literature data on real-life practice patterns in the management of severe asthma in Turkey and agreed on a series of statements supported by scientific evidence and expert clinical opinion. The local ethics committee of Ankara University, School of Medicine, approved the study (Approval number: 14-685-16)

Cost analysis

Average per patient direct medical costs were calculated based on cost items outpatient visits, laboratory and radiological tests, hospitalizations/interventions, drug treatment/equipment and co-morbidities from payer perspective (only direct medical costs using prices of the public payer "Social Security Institution (SSI)" in Turkey), using cost of illness method developed by WHO (32). For drugs, retail prices from the updated price list and updated institution discount list of SSI for May 2016 were taken into account in calculation of the unit costs (33). Average usage rate for active ingredients was calculated based on data provided by each clinic regarding percent use of active ingredients, while the average of all brands included in the current reimbursement system was calculated using the unit costs. Costs related to diagnostic tests were calculated considering the Health Implementation Notification by SSI (34). Physician visits costs were calculated using unit prices also based on the same SSI notification (34). Salaries and labor force of healthcare staff giving service to pediatric asthma patients was provided from the Healthcare Organization Questionnaire composed of Staff Inventory Form and Information Form on the Labor Force Spent during an intervention filled for each study center. Hospitalization costs were calculated using unit prices based on Healthcare Organization Price List in Health Practice Declaration and Treatment Assist Practice Declaration. Monetary results were converted by using

2.97 USD/TL May 2016 exchange rate. Direct non-medical costs of different origin (*e.g.*, transfers of patient and caregivers for examinations and/or hospitalization, home care, *etc*.) and indirect costs were not included in the cost analysis. For each cost item, calculation was based on the formula:
Percentage of patients utilizing the item x number of item utilization x unit cost.
Total cost was reached via sum of all cost items.

Statistical analysis

Descriptive statistics were used to summarize results on practice patterns for the pediatric asthma management. Expenses related to management of pediatric asthma were the main cost-analysis related parameter of the study. Cost model was based on the following equation: *Cost* = $\sum$ *(Frequency; %) x (Unit price; TL) x (patient ratio; %).*

Results

Overall patient profile

The present cost of illness study was based on expert panel opinion regarding practice patterns in the management of severe asthma in Turkey and included overall 25,579 patient admissions (severe asthma in 21.25%) per year from 14 clinics across Turkey. Accordingly cost calculations were based on the prevalence of severe asthma (21.25%), rates of controlled (32.56%), partially controlled (40.06%) and uncontrolled (27.39%) disease in severe asthma patients, prevalence of severe asthma in patients with severe asthma attack (60.83%), rates for controlled (30.0%) and uncontrolled (55.33%) disease in severe asthma patients with severe asthma attack and percentage (72.50%) of acute asthma attacks in patients with severe asthma being treated with hospitalization.

Outpatient admission cost item

Outpatient admission was estimated to occur in 100.00% of patients and for 11 times per patient per year at Pulmonology and Allergy and Immunology Diseases outpatient clinics, in 34.2% of patients at Cardiology, in 29.5% of patients at Ear Nose and Throat and in 27.4% of patients at Endocrinology outpatient clinics, each for once a year per patient. Acute asthma attack was considered to be associated with admission to Pulmonology and Allergy and Immunology Diseases outpatient clinics in 50.3% of patients and for 4 times per patient per year (**table I**).
Based on unit costs, total per patient annual cost related to outpatient admissions was calculated to be $ 177.91 (**table I**).

Laboratory and radiological tests cost item

Most common laboratory tests were considered to be spirometry (99.7%), PA/lateral chest X-ray (94.8%) and reversibility test (95.9%) during attack-free period, while respiratory function test (91.4%), reversibility test (82.5%) and skin prick test (84.5%) during an acute asthma attack. High resolution lung CT (56.0%) and lung CT (35.7%) were the most commonly required radiological tests in attack-free period and during an acute asthma attack, respectively (**table II**).
Based on unit costs, total per patient annual cost related to laboratory and radiological tests was calculated to be $ 82.32 (**table II**).

Table I *- Outpatient admission cost item: clinical practice, unit costs and total cost.*

Outpatient admissions	Annual admission rate (%)	Annual visit # per patient	Unit cost per admission ($)	Total cost
Pulmonology and allergy and immunology diseases	100.0	11	13.39	147325.10
Ear nose and throat	29.5	1	2.02	595.56
Endocrinology	27.4	1	2.02	554.14
Gastroenterology	2.5	1	2.02	50.51
Rheumatology	2.9	1	2.02	58.99
Cardiology	34.2	1	2.02	691.72
Psychiatry	17.1	1	2.02	345.05
Ophthalmology	14.9	1	2.02	301.41
Physical therapy and rehabilitation	21.4	1	2.02	432.12
Chest diseases (acute attack)	50.3	4	13.39	26925.67
Emergency (acute attack)	3.1	4	5.22	643.01
Total				177923.28
Per patient outpatient admission costs ($)				**177.91**

Hospitalizations/interventions cost item

Hospitalizations were considered to occur twice in a year at ward in 39.8% of patients (each for 8 days) and at ICU in 1.5% of patients (each for 4 days) with severe asthma during attack-free period. Overall, a patient with severe asthma was considered to have 4 attacks per year and 3 attacks per year (72.5% of total attacks) were considered to result in hospitalization. Hospitalization for an acute attack was considered to occur tree times in a year at ward in 47.6% (8 days for each) and at ICU in 2.1% (1 day for each) of patients with severe asthma (**table III**).

Based on unit costs, total per patient annual cost related to hospitalizations and interventions was calculated to be $ 1,154.55 ($ 525.1 for attack-free period and $ 629.5 for acute asthma attack related hospitalizations) (**table III**).

Drug treatment and equipment cost item

Based on prescription rates in Turkey, maintenance doses and annual dose and unit cost per box for each drug regimen and unit costs of equipment, total per patient annual cost related to drug treatment and equipment was calculated to be $ 2,289.63 ($ 2,199.7 for attack-free period and $ 89.8 during acute asthma attack) (**table IV**).

Co-morbidities cost item

Most common co-morbidities in severe asthma patients in Turkey were considered to be rhinitis (47.4%), reflux (43.8%), sinusitis (42.2%) and allergic rhinitis (33.3%). Based on prevalence of comorbid disorders in patients with severe asthma in Turkey and related unit costs, total per patient annual cost related to co-morbidities and complications was calculated to be $ 665.39 (**table V**).

Per patient total annual direct medical cost

Based on total annual per patient costs calculated for outpatient admission ($ 177.91), laboratory and radiological tests ($ 82.32), hospitalizations/interventions ($ 1,154.55), drug treatment/equipment ($ 2,289.63) and co-morbidities ($ 665.39) cost items, total per patient annual direct medical cost related to management of severe asthma was calculated to be $ 4,369.76 from payer perspective (**table VI**).

Drug treatment/equipment (52.4%) was the main cost driver in the management of severe asthma in Turkey, as followed by hospitalizations/interventions (26.4%) and co-morbidities (15.2%) (**table VI**).

Discussion

Our findings revealed that per patient annual direct medical cost of severe asthma in Turkey was $ 4,369.76 from payer perspective and drug treatment ($ 2,289.63; 52.4%) was the major cost driver as followed by hospitalizations ($ 1,154.55; 26.4%) and co-morbidities ($ 665.39; 15.2%). Drug treatment cost was higher for attack free period as compared with acute attack ($ 2,199.7 *vs* $ 89.8), while anti-IgE treatment was responsible for 83% of the medication cost during attack-free period.

Annual direct per patient medical cost for severe asthma was reported to be $ 658 in Thailand (35), $ 135 to $ 733 in Brazil (17), $ 1277 in Spain (14), $ 1563 in previously in Turkey (36), $ 1635 in South Korea (20), $ 2214 in Korea (16), CHF 3075 in Switzerland (31), VND 13,196,280 in Vietnam (37), € 2635 in Spain (38), $ 6354 in USA (28), € 8221.5 in France (39), while estimated at $ 4369 in the present analysis.

In a systematic review of 29 cost-of-illness studies of asthma, the annual incremental socio-economic cost of asthma was reported to range from € 416 to € 5,317 in adults and to further increase with level of severity from € 964 for intermittent asthma to € 11,703 for severe persistent asthma (40). Authors concluded that a large variation exists in the severe asthma costs per affected person by country limiting their comparability (40). This seems consistent with the similarly non-uniform data regarding the total annual asthma costs between countries that ranges from $ 346 in the USA and US $ 1,395 in Sweden (14, 28). Notably, the assessment of asthma burden is considered a challenge with remarkable variations in asthma prevalence and disease severity within and among countries even with use of similar research protocols (41).

Our findings revealed medications (52.4%) to be the main cost driver in severe asthma, particularly in the attack-free period, while hospitalization (26.4%) was the second-most contributor to overall direct cost, particularly during acute exacerbation. This supports that prescription medications rather than hospitalizations comprise the largest percentage of total costs attributable to asthma in the adult population (42-44).

In a retrospective analysis of a national administrative claims database in USA, authors reported that an increased mean annual asthma-related costs in severe versus persistent asthma ($ 6,496 *vs* $ 2,739) which was shown to be driven mainly by 3-fold greater mean annual asthma medication costs in severe asthma, while twice as many asthma-related hospitalizations in severe asthma represented the second largest category of asthma-related costs (18).

Likewise, total per-person direct annual costs of asthma were reported to be $ 3180 in USA with medications ($ 1605; 50%) rather than hospital admissions ($ 463; 15%) accounted for the largest share of direct costs (39). However, subgroup analysis of patients with severe asthma revealed direct per patient medical cost to be $ 6354 with consideration of both medications ($ 2404) and hospitalizations ($ 2122) as the major cost drivers (39). Similarly, in a systemic review of cost of severe asthma in Brazil, average annual direct costs per patient for severe asthma was reported to range from $135 to $ 733 from public health system perspective and to range from $ 764 to $ 929 from the family perspective with hospitalizations and medications indicated to be the key cost drivers of severe asthma (17).

Drug cost and hospitalization were also documented to be main cost items responsible for the burden of severe asthma on health

Table II *- Laboratory and radiological tests cost item: clinical practice, unit and total cost.*

Laboratory/radiological tests	Annual rate (%)	Annual test # per patient	Unit cost ($)	Total cost ($)
At diagnosis				
Spirometry	99.7	1	8.42	8395.08
Complete blood count	92.9	1	0.00	0.00
PA/lateral chest X-ray	94.8	1	0.00	0.00
Reversibility test	95.9	1	0.00	0.00
Sputum smear	10.8	1	0.00	0.00
High resolution lung CT	56.0	1	18.52	10372.36
DLCO	41.1	1	14.98	6153.41
Specific IgE measurement	29.4	1	7.14	2097.85
Serum total IgE measurement	81.5	1	0.00	0
Skin Prick Test	89.9	1	20.21	18163.11
Sinus CT	37.0	1	18.52	6848.24
Eosinophil count	95.1	1	0.00	0
BMD	26.5	1	7.00	1852.34
During follow up				
Respiratory function test	91.4	1	8.42	7693.87
Reversibility	82.5	1	0.00	0
Bronchial provocation test	3.6	1	12.90	460.61
Exhaled CO measurement	10.7	1	8.42	901.55
Lung CT	35.7	1	18.52	6614.91
Skin Prick test	84.5	1	0.00	0
Sweat test	0.5	1	11.41	61.64
Specific IgE measurement	25.3	1	0.00	0
Lung MRI	0.6	1	21.89	129.12
Bronchoscopy	8.5	1	50.34	4258.52
Tuberculin test	1.2	1	0.00	0
Bronchial biopsy	2.6	1	77.03	2010.46
Lung volume diffusing capacity	35.7	1	14.98	5350.33
Arterial blood gas analysis	32.3	1	0.00	0
Exercise test	4.25	1	10.00	424.96
Alpha-1 antitrypsin test	3.0	1	2.79	84.98
Theophylline level	3.9	1	4.71	185.26
Endoscopy	22.1	1	33.70	74.34
BMD	13.1	1	0.0	44.21
High resolution lung CT	41.7	1	18.52	140.27
Total				82317.42
Per patient laboratory and radiological tests cost ($)				**82.32**

BMD: Bone mineral density; CO: carbon monoxide; CT: computerized tomography; DLCO: Carbon monoxide diffusing capacity; Ig: immunoglobulin; MRI: magnetic resonance imaging; PA: posteroanterior.

Table III - *Hospitalization/interventions cost item: clinical practice, unit costs and total cost.*

	Annual # of hospitalization	Rate (%)	LOS per admission (days)	Unit daily cost ($)	Total cost ($)
Attack-free period					
Pulmonology ward and allergy and ICU	2	39.8	8	73.19	465715.15
immunology	2	1.5	4	503.69	59292.26
Diseases chest total					525007.07
For an acute attack					
Pulmonology ward and allergy and ICU	3	47.6	8	73.19	835953.54
Immunology	3	2.1	1	503.69	32380.47
Diseases chest total					629542.14
Total					1154549.36
Per patient hospitalization cost ($)					**1,154.55**

ICU: Intensive care unit, LOS: Length of hospital stay.

economics in a past from Turkey which evaluated the direct costs of asthma in the same patient group within eight years interval (36). Authors reported no significant difference from 2000 to 2008 in mean annual asthma cost ($ 659.8 *vs* $ 830.2) and in the cost increment due to severe asthma ($ 1563 *vs* $ 152.8 for mild and $ 857.4 for moderate asthma), while drugs (45%) and hospitalization (40%) were reported to be the main components of the direct costs (36).

Contribution of attack-free disease to the majority (96%) of total drug costs in the present study supports the reported increase in the percentage of total cost attributable to hospitalization (from 4% to 48%) and decrease in the percentage of total cost attributable to drugs (from 46% to 26%) with decrease in asthma control level in Turkey (30). A decline in the percentage (from 47% to 19%) of total costs attributed to medications as the disease severity increases from mild to severe was also reported in asthma patients from USA (28).

This seems also to be in agreement with findings from a past study on the economic burden of asthma in Asia-Pacific region which revealed maintenance costs (medication, physician visits) in controlled asthma, whereas higher urgent care costs (emergency care and hospitalizations) in case of poor asthma to be the main driver of asthma-related costs (45).

Notably, analysis of costs by disease severity and exacerbation status in asthma patients from Switzerland revealed attribution of medication and hospitalization costs to 70.4% and 9.6% of total cost, respectively in patients without exacerbations, while to 28.1% and 63.4% of total costs, respectively in patients with exacerbation (31). Accordingly, our findings emphasize medications as the main cost driver predominantly in the attack-free period with the cost of drugs approximately doubling the cost of hospitalization for severe asthma. Although these findings support the consideration of asthma drugs to account for most of the incremental ($ 1056) per patient annual direct costs attributed to severe uncontrolled asthma (46), it should be noted that addressing the biologic use is important in cost-analysis of managing patients with severe asthma who are the primary target for biologic therapies (47). Although biologics have been reported to be associated with decrease in the frequency of asthma exacerbations, unplanned health care use, including emergency admissions and hospitalizations in clinical trials with severe asthma patients (48), the major concern about use of biologics is the cost (49). Data from pharmaceutical manufacturers indicated the wholesale acquisition cost of an individual unit of these biologics to range from $ 879 to > $ 47502, while ICER report recommended that biologic costs would need to be reduced 62% to 80% from their 2018 wholesale acquisition cost, depending on the biologic, to meet the cost-effectiveness threshold (50). Hence, the cost of omalizumab (the only biological drug available in the current study), calculated based on local references (51-53), contributed to 83% of overall medication cost in the attack-free period in our study. This seems notable given that cost-effectiveness data for omalizumab revealed wholesale acquisition cost to be $ 39,048 and discount from WAC required to achieve cost-effectiveness threshold prices to be 66-77 % (49). Nonetheless, the sustainability of biological drugs is considered doubtful and difficult to be demonstrated, if the payer does not take into account the indirect and intangible costs.

It should be noted that the 72.50% of acute attacks in severe asthma patients were considered to be treated by hospitalization in the present cost analysis. Given that the smaller proportion in hospital costs and the higher proportion in medication costs is considered suggestive of better control of asthma (6), significant contribution of experiencing exacerbations to total hospitalization costs but not

Table IV *- Drug treatment and equipment cost item: clinical practice, unit costs and total cost.*

Attack-free period					
Equipment	**Patients (%)**	**Duration**	**# of equipment**	**Unit cost ($)**	**Total cost ($)**
Peak flow meter	23.1	1/year	1	0.00	0
Nebulizer	53.2	1/year	1	0.45	241.64
Drugs	**Prescription (%)**	**Daily dose**	**Duration**	**Unit cost (box/year; $)**	
SABA	85.2	According to posology		31.89	27154.77
LABA + ICS	99.9			150.98	150869.78
Systemic steroids	27.0			22.71	6137.06
Leukotriene antagonists	69.9			104.32	72882.33
SAMA	17.5			314.31	55003.47
Triotropium/LAMA	30.1			170.80	51446.79
Theophylline SR	17.1			30.76	5265.43
Theophylline FA	7.8			57.58	4478.11
Anti-IgE	26.1			499.51	1826147.74
Clarithromycin	1.9			8.81	166.76
Total (attack free)					2199793.89
For acute attack					
Nebulized ICS	64.6	According to posology		11.00	7108.18
Systemic steroids	97.1			3.91	3797.95
LABA-FA	37.1			7.69	2857.47
ICS/LABA	45.4			13.39	6073.43
SABA	100.0			3.10	3103.37
SAMA	72.9			4.31	3136.91
Theophylline FA	43.6			1.55	673.68
Magnesium sulphate	24.8			17.06	4221.82
Total (acute attack)					89821.10
Total					2289614.99
Per patient drug/equipment cost ($)					**2,289.63**

ICS: Inhaled corticosteroids; FA: fast-acting; Ig: Immunoglobulin; LABA: Long-acting beta-2 agonists; LAMA: Long-acting muscarinic antagonist; SABA: Short-acting beta-2 agonists; SAMA: Short-acting muscarinic antagonist; SR: slow release.

to medication costs in severe asthma patients in our analysis seems to emphasize the likelihood of inappropriate treatment and failure to reach targeted treatment intensity recommended by guidelines in a considerable portion of patients with severe asthma (54, 55). In a cost of illness study estimating the direct cost per asthma exacerbation in Turkey, high hospitalization rates reported in patients with asthma attack was considered to be highly suggestive of unnecessary and inappropriate hospitalization since asthma attack was mild to moderate in more than 75% of patients (21). Given that asthma attacks leading to hospitalization account for 90% of the total costs of attacks (56), our findings emphasize the likelihood of a cost-saving with appropriate hospitalization and better management of asthma attacks in severe asthma patients, since effective implementation of best practice results in significant cost savings in asthma management (57). Presence of co-morbidities were reported to be associated with significant cost increment in asthma patients along with consideration of even low-cost high prevalence diseases such as lower respiratory tract infections as significant cost drivers (6, 31, 58, 59). Accordingly, in our analysis co-morbidities (26.4%) were the third largest category of asthma-related costs following the medication and hospitalization costs in patients with severe asthma.

Table V - *Co-morbidities cost item: clinical practice, unit costs and total cost.*

Comorbidities	Patients (%)	Unit cost ($)	Total cost ($)
Rhinitis	47.4	26.34	12486.92
Allergic rhinitis	33.3	157.43	52358.69
Sinusitis	42.2	19.68	8306.75
Polyp	20.4	331.39	67438.85
Reflux	43.8	228.51	100104.60
Hypertension	33.4	58.06	19393.85
Obesity	10.6	0.00	0.00
Sleep apnea	5.9	926.82	54285.41
Psychiatric disease	17.7	91.52	16158.78
CAD	2.9	345.19	9862.70
Rheumatic disease	2.1	5.22	107.45
Cataract	2.4	138.05	3253.97
PID	0.8	38815.49	321614.04
Total			665372.03
Per patient comorbidities cost ($)			**665.39**

CAD: Coranary artery disease; PID: Primary Immune Deficiency.

This seems notable given that in a systemic review of 68 cost-of-illness studies of asthma, disease severity and presence of co-morbidities were found to be indicated amongst the factors that can contribute to higher total hospital costs by studies which revealed hospitalization as the major cost driver of direct asthma costs (6). Certain limitations to this study should be considered. First, being focused only on direct costs, lack of data on indirect costs (loss of productivity due to the illness) or intangible costs of illness (costs of suffering for the patient and his/her family) seems to be the major limitation of the present study which likely to result in a downward bias in our estimates of the economic cost of severe asthma. Second, use of expert consensus based data rather than national database on practice patterns to identify direct medical costs might raise a concern with the validity and reliability of the data. Third, while a cost-of-illness study gives a perspective on the economic burden of asthma in a population, it does not reflect what is happening with the individual patient or family unit. Fourth, cost analysis was based on severe asthma care in tertiary care centers and therefore practice patterns and related contribution to overall of direct cost of severe asthma may differ from non-tertiary care centers. Nevertheless, providing cost estimates for management of severe asthma patients with respect attack-free and attack periods in Turkey, our findings represent a valuable contribution to the literature.

Conclusions

In conclusion, our findings indicate that managing patients with severe asthma pose a considerable burden to health economics in Turkey, with medications as the main cost driver, particularly in the attack-free period alongside the likelihood of hospitalization to account for a larger share of costs in patients with acute exacerbation. Hence, our findings emphasize the likelihood of cost-savings with implementation of appropriate hospitalization practices, more effective strategies to prevent asthma attacks and to improve asthma control status as well as with better management of asthma attacks in severe asthma patients. Future studies addressing both direct and indirect costs of severe asthma with the potential impact of factors such as patient adherence, inhaler techniques or smoking on cost estimates may help to extend the knowledge about the impact of severe asthma on functioning and quality of life and morbidity at individual and family level and to develop cost-effective strategies in the disease management.

Acknowledgments

The creation of the model used in this study, statistics and editorial support were sponsored by GlaxoSmithKline, Turkey in the context of unconditional scientific support. GlaxoSmithKline, Turkey has not contributed to the content of the study. Authors

Table VI - *Per patient annual direct medical cost related to management of severe asthma.*

Cost items	Per patient annual cost ($)	Contribution to total cost (%)
Outpatient admission	177.91	4.1
Laboratory test	82.32	1.9
Hospitalization/intervention	1,154.55	26.4
Drug/equipment	2,289.63	52.4
Comorbidities/complications	665.39	15.2
Total direct per patient cost ($)	**4,369.76**	

would like to thank Cagla Ayhan (MD) and Sule Oktay (Prof., MD, PhD) from KAPPA Consultancy Training Research Ltd (Istanbul, Turkey) who provided editorial support; Doctors Emine Gullu Arguder, Ayse Baccioglu, Sibel Atis, Berna Dursun, Ferda Oner Erkekol, Fusun Kalpaklioglu, Secil Kepil, Sadan Soyyigit and Insu Yilmaz who provided data for the study and Yalcin Seyhun (MD, PhD, Senior Medical Lead) and Gizem Saribas (Market Access & Pricing Manager) from GlaxoSmithKline, Turkey.

Conflict of interests

The authors declare that they have no conflict of interests.

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