Cost analysis of childhood asthma in Iran: A cost evaluation based on referral center data for asthma and allergies

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Objective: Asthma as the most common chronic disease in childhood reduces the quality of life of children and their families. We aimed to estimate the cost of managing childhood asthma in Iran and to examine its variability depending on asthma severity.

Methods: The cost of asthma was estimated by building a cost assessment model regarding the factors that influence the cost of asthma in children including age and sex distribution, prevalence of disease severity, level of resource utilization depending on disease severity (3 groups of controlled, partly controlled and uncontrolled were defined). The model was comprised of both medical (cost of medication, physician visit and respiratory tests) and non‑medical (transportation and hoteling) costs. Furthermore, the average family income in each category was figured and the share of asthma managing costs from the average income was calculated in different groups.

Findings: According to model, the total cost of childhood asthma in Iran was around 516.5 million dollars. Moreover, direct medical cost represented 49% of the total costs, among which 66% accounting for medication cost. Direct non‑medical costs were estimated 51% with the majority (93%) expended on transportation. In addition, the mean annual cost per child was approximately 466 dollars. In addition, the results indicate the vast majority of patients (46%) are categorized in the uncontrolled group.

Conclusion: The cost of childhood asthma in Iran is extremely high comparing to the average income of Iranian families in all categories of asthma severity. Considering the high amount of transportation cost, the accessibility of asthma treatment does not appear to be acceptable. The major source of costs is found to be related to medicine expenditure. Since it has been proven that using medicine does not necessarily result in a well‑controlled disease status, alternative approaches should be considered in asthma management.

Keywords: Childhood asthma; cost analysis; pharmacoeconomics; Iran

INTRODUCTION

Asthma is one of the most common chronic diseases world-wide and in all age groups, which yearly impose considerable costs to the countries health system.¹ On the other hand, the health care cost growth rate is now overtaking of gross domestic product.² Due to the uncontrollable nature of asthma disease and its increasing in prevalence and severity, costs imposed on society and patient will be higher by the day. Therefore, better control of the disease significantly reduces the costs.³ Assessing the quality of life in asthma patients shows a strong effect on the economic and social not just on patients, but also affects the whole family.³ Asthma is estimated to be the first cause of absence from school, need for emergency care and hospitalization in children. ⁴ It is estimated that the world-wide prevalence of asthma has increased almost 50% during the past 10 to 15 years. At present, global rate of asthma patients is 300 million. Moreover it is predicted by
2025, 100 million be added to the population of the world’s asthma patients.\textsuperscript{[9]} Over the past decade, most of the controlled studies show that asthma prevalence in children has increased annually 5-6% and doubled in the last 20 years.\textsuperscript{[6]}

According to the global burden of asthma in 2003, the average prevalence of symptoms in Middle East children was 10.7%. The reported range for the prevalence of symptoms starts from 7.5% in Morocco to 17% in Kuwait.\textsuperscript{[7]} Based on the mentioned report, prevalence of asthma in Iran was about 5.5% in total population and 10% in childhood. However the second report of this committee in 2004 showed the prevalence of asthma symptoms in children, in Iran, was 13.2% which demonstrated an increased rate of 0.17% in common symptoms.\textsuperscript{[8]} The average prevalence of asthma symptoms in people under 18 years in Iran is 13.14%. Therefore considering the changing pattern of in society, if the trend of asthma prevalence continues in the mentioned rate, it will be well over 15% of the border until the year 2013. According to the importance of this subject in developing countries, it is necessary to estimate direct and indirect costs imposed on asthma patients. Based on the studies conducted in Iran in 2001 total costs of asthma and allergy treatment containing drug costs, was 13.1 million dollars which was equal to 4% of the total drug of administration in the country.\textsuperscript{[9]} Taken collectively, the effective and efficient deployment of resources allocated to the pharmaceutical products and services and also analysis of resulting clinical, economic and humanistic outcomes attaches great importance, which in turns requires designing of systematic studies in the field of the drug economy. In this regard, this study aimed to estimate the costs of childhood asthma in Iran and its relationship to the severity of disease. It should be noted that the study has been conducted from the perspective of patients.

**METHODS**

Data of 72 children under 16 years as qualified cases was calculated using population data on Children’s Medical Center (CMC) as a referral center of asthma treatment in Iran. Clinical data was obtained from medical records of patients archived at the office of a physician with well-established expertise in children asthma. Patients’ data were collected based on two separate forms. In the first questionnaire, demographic variables were investigated including: age, gender, home address, phone, birth weight, duration of breastfeeding, family size, parental occupation, family income, type of insurance, costs related to travelling, hoteling and accommodation, clinical history including disease duration, asthma and allergy medications and the history of other respiratory tests and finally therapeutic regimen prescribed by a physician for the patient and its related costs. Second form was asthma control test questionnaire based on the global initiative for asthma (GINA)\textsuperscript{[9]} which filled by the patient’s parent. Asthma was diagnosed by a specialist based on GINA 2009 guidelines\textsuperscript{[10]} and its severity was determined by the 2\textsuperscript{nd} number. This questionnaire measures asthma severity in accordance with the grading plan of responses to questions that indicates the status of the patient during the last month. Children were divided in terms of disease severity to three groups of controlled, partial controlled and uncontrolled. If the total score was 27, patients were placed in the control group, the score between 17 and 25 were patients of partial control the score less than 17 was belong to the uncontrolled group. The cost of the drugs prescribed by the physicians was collected from a referral pharmacy in Tehran. After the 1979 Islamic revolution, Iran has adopted a full generic-based medicine system and local production of essential medicines and vaccines has become one of the main goals of the national drug policy.\textsuperscript{[11,12]} In the cases of that physicians have had emphasized on the use of some brand medications, such as oral sprays such as Seretide\textsuperscript{®} and Flixotide\textsuperscript{®} and also Nasonex\textsuperscript{®} nasal spray and Zaditen\textsuperscript{®} syrup, the price was calculated in the base of the original brand price, but in the case of other medications such as Salbutamol oral spray, Salmeterol, Beclomethasone, Cromolyn nasal spray, Cetirizine tablets and syrup, Loratadine and Ketotifen tablets Iranian drug costs were considered.

The cost of asthma was estimated by building a cost assessment model regarding the factors that influence the cost of asthma in children including; age and sex distribution, prevalence of disease severity, level of resource utilization depending on disease severity (Three groups of controlled, partly controlled and uncontrolled were defined). Clinical and cost data were collected from medical and cost records preserved at CMC and a referral pharmacy, respectively [Table 1]. The costs have been updated to year 2012 (1 United States of America’ Dollar

**Table 1: Maximum and minimum values for direct medical and non-medical costs (unit cost of resources)**

| Cost category          | Maximum price ($) | Minimum price ($) |
|------------------------|-------------------|-------------------|
| Medications            | 49.592            | 0.012             |
| Physician visit        | 5.098             | 5.098             |
| Respiratory tests      | 18.903            | 18.903            |
| Transportation         | 611.746           | 0                 |
| Hoteling               | 203.915           | 0                 |

Prices are presented as United States Dollar
Furthermore the average family income in each category was figured and the share of asthma managing costs from the average income was calculated in different groups. Inclusion criteria for this study set as following:

- Diagnosis of asthma with Specialist in children asthma and allergies
- Patient’s willingness to participate in the study
- Collaboration in completing the questionnaires
- Proper and regular use of medication
- Responding to telephone inquiries of researcher a month after visiting at the Medical Center of Monitoring.

Cases which did not follow recommended medication/drug regimens because of human or economic burden of those conditions were excluded.

RESULTS

A total of 72 patients were included in our study. Of these, 13 patients were in the control group. There were 26 patients in the partial controlled group and 33 patients in the uncontrolled group. From a total of 72 patients participated in the study, 51 patients (71%) were males and 21 (29%) were female. The mean age of patients was 6.68 ± 2.83 years and age range of the patients was under 16 years. The highest percentage of 39% was allocated to the age range of 6-9 years. In summary, 41 patients (57%) were from Tehran (The capital city of Iran) and 31 patients (43%) were referred from other cities to Children’s Medical Center. Nineteen children (26%) have been delivered normally and 34 children (47%) have been delivered by cesarean section. Regarding travelling, among these patients, 40% by private vehicle, 25% by taxi, 24% by public vehicles such as buses or subways have travelled in the city of Tehran and in the case of patients from other cities 3% by plane and 8% by bus were traveling to Children’s Medical Center. About 49% of participants have had family income less than 407 dollars and 10% had no health insurance [Table 2]. In this study, the mean of total direct medical costs was 619.38 ± 15.5$, the average drug cost was 408.00 ± 13.15 (66%), the mean of patient visits costs was 91.74$ (15%) and the average cost of the respiratory test was 119.76 ± 9.1 (19%). The mean of total direct non-medical cost was 638.76 ± 134.4$ which is related to average travel expenses as 601.68 ± 124.08 (93%) and 37.08 ± 24.08 (7%) which is related to the average cost of hoteling [Table 3 and Figure 1].

DISCUSSION

In this study, the average annual cost of asthma per child person was estimated 466.8$ (258.18$ for mild asthma and 607.75$ for severe asthma respectively). Considering the prevalence of asthma in Iran (5/1-7/5%) according to a report from GINA in 2004[14] the total annual cost of asthma treatment was 516,468,560$ (the total annual cost of asthma treatment is 418,093,596$ if the prevalence of asthma is considered 5/1% and 614,843,524$ if the prevalence of asthma is taken up 7/5%). Furthermore, we showed that the average annual costs related to direct non-medical costs was 51% (285,456,961$) and the average of direct annual costs was 49% (231,011,598$) [Figure 2]. In this regard, it has been reported in developed countries that the total cost of asthma per person is in the range of 326-1,315 dollars.[15]

This is the first time that the costs of asthma management have been estimated in Iranian setting, which can be considered useful for policymakers and further investigations on the topic. Nonetheless, the results of this study should be interpreted in light of several limitations. First, this study was conducted...
as a single-center study that restricts the reliability of generalized figures. It could be suggested that more severe case patients have been referred to this center for treatment, thus overestimating the costs in this specific group. Secondly, some of indirect costs such as absenteeism were not included that could have influenced the overall costs in another way.

According to Blasco Bravo et al. (2011), it has been estimated that the social cost caused by handling asthma in children between 16 years in Spain in 2008 was very high, some 532 million Euros and can vary between 392 and 693 million Euros. Most of the costs are direct costs of asthma (60.1% of the total cost) and although many publications do not refer to the indirect costs, in this study represent 39.9% of the total cost. The average annual cost of asthma for asthmatic infants is 1149 Euros and ranges from 403 Euros for milder severity category to 5380 Euros for the most serious. To reduce the cost of childhood asthma should realize interventions in prevention and

Data are presented as N (%), unless otherwise specified. SD: Standard deviation

Table 3: Estimate value for average direct medical and non-medical costs per year per patient in each group

| Mean costs related to | Controlled | Partial controlled | Uncontrolled | Total |
|-----------------------|------------|--------------------|--------------|-------|
| Medications           | 127.80±12.5| 130.80±12.6        | 150.00±13.8  | 408.00±13.1 |
| Physician visit       | 30.54±0    | 30.54±0            | 30.54±0      | 91.74±0 |
| Respiratory tests     | 43.62±9.6  | 34.92±8.9          | 41.22±9.2    | 119.76±9.1 |
| Direct medical costs  | 201.72±14.0| 196.14±14.1        | 221.58±17.3  | 619.38±15.5 |
| Transportation        | 56.46±27.9 | 196.08±95.2        | 349.08±161.2 | 601.68±124.0 |
| Hoteling              | 0          | 0                  | 37.08±35.5   | 37.08±24.0 |
| Direct nonmedical costs | 56.46±27.9 | 196.08±95.2        | 386.16±178.0 | 638.76±134.4 |
| Direct medical and nonmedical costs | 258.18±28.2 | 392.22±93.3        | 607.74±176.8 | 466.80±133.5 |

Prices are presented as United States Dollar.
in the disease management as a very important both the cost and years with persistent asthma is due to preventable causes, such as hospitalizations and care emergency department.[16]

Based on our results, although the population of patients with uncontrolled asthma was more than other groups, however the direct treatment and non-treatment costs was consistently increased by increasing disease severity, so that the mean total cost of treatment in the uncontrolled group, was 2.4 and 5.1 times greater than that of controlled and partially controlled groups respectively. Moreover, the average direct nonmedical costs in uncontrolled group were 6.8 and 2 times greater than that of controlled and partial controlled respectively. In addition, there was not significantly difference in terms of average direct costs of treatment in three groups [Figure 3].

Other related studies, which had also included the costs of hospitalization, have shown that hospitalization costs and medical costs are two major costs of asthma treatment. Prescription of corticosteroids and training of patient and his family result in decreasing hospitalization costs.[17]

The increase in the cost of asthma is reported to be mainly due to uncontrolled severe disease.[18] Confirming our results which shows a positive correlation between overall costs of asthma and its severity, Celik et al. (2004) have shown that 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.[15]

Consistent with our results, medications were found to be the major contributor to the cost of asthma. In a large-scale study, the costs of asthma medication were found to be the largest cost factor in children (382.09$ or 41.3% of total direct cost). Furthermore, according to the results of 18 studies, drug expenditures have been introduced as the largest portion of direct costs accounting for 38-89% of total costs.

In view of the fact that the patients were referred to the out-patient clinic, therefore the costs of emergency treatment and hospitalization costs were not calculated in this study. In the present study, medication cost constituted 32% and 66% of the majority of direct medical costs and total medical expenditures respectively. This figure is higher than in previous studies, which report that drug costs make up 30-40% of the total direct cost of asthma.[17]

A reasonable explanation for this difference could be due to the newer and more expensive asthma drugs such as inhaled corticosteroids, long-acting inhaled β2-agonists and leukotriene modifiers compared with the previously used medications or it might be also due to lower unit cost of diagnostic tests and physician visits in our country compared with the other countries.

In our study, the total cost of medication in children with moderate and severe asthma, was three times and twice higher than that of children with mild asthma. As a rational reason it may be due to the number of children with moderate and severe asthma, which were 3 and 2 times more than the number of children with mild asthma. Therefore in view of the fact that the average cost of medications in all groups were close together, so the only factor could be the large number of the population of children with uncontrolled asthma, which cause the increase in drug cost with increasing asthma severity. These findings may indicate that intervention strategies targeting the treatment and control patients with uncontrolled asthma can reduce costs.

In the present study, direct nonmedical costs included traveling and hoteling costs of asthmatic children. In five studies, the indirect costs greatly exceeded the direct costs accounted for 52-75% of the overall costs.[17] In the present study, although the costs due to the absence from school (school days lost) have not been determined (because of the low accuracy in calculating), but the portion of direct nonmedical costs (51%) was higher than the direct costs (49%).

Evaluating the direct nonmedical costs it was determined that private vehicle; public means of transportation and plane have been used by 40%, 6% and 2% of the patients respectively to transfer from the personal location to the medical center. In this regard, travelling cost was detected as the greatest portion of the expenditures of asthma treatment so that 93% of direct nonmedical costs and 48% the total cost was allocated to it. Based on our survey, children with asthma who travel from other cities to Tehran to access treatment, is 33.3% which is relatively high. Therefore, facilitation in accessibility to specialist and medications needed to treat is extremely important in

Figure 3: Comparison of direct medical and non-medical cost percentage in different groups
Iranian cities and certainly if there are special clinics for asthma and attending physicians in these centers and easy access for patients to specialist will lead to a significant reduction in direct nonmedical costs.

Although epidemiological studies have no definitive conclusion about the causal effect of air pollutants on asthma induction, but several evidences support a causal relationship between exposure to air pollution and exacerbation of asthma, mainly due to exposure to particulate matter and ozone.\[^{[9]}\]

In this study, compared with other provinces the most number of referring patients were from Tehran (66.7\% of evaluated patients) and Alborz (16.7\% of evaluated patients). This was predictable as Tehran and Alborz are the most polluted provinces of Iran and a 35\% prevalence of asthma symptoms in Tehran. Therefore, planning for pollution control and educating the patients with asthma can lead to lower costs.

Several studies have shown that asthma prevalence in the population less than 16 years is more in boys than girls. In our study, the prevalence of asthma in boys was more than double that of females. According to our results, in the severe asthma group (uncontrolled group), the population of boys was almost twice greater than that of girls which shows asthma is more severe in young boys.

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. As is true of any study, there are limitations in the economic analysis of diseases and one must be cautious in the interpretation of the results. Our findings might suggest that intervention strategies targeting severe asthma patients could decrease the cost of the disease in the population. 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.

The following reasons suggest that asthma costs in Iran can be higher than the amount that was announced in our study:

1. Not calculated hospitalization costs as direct costs and direct non-medical costs of absenteeism from school
2. Even though the cost of medicines throughout the country is invariable due to the policies of the Ministry of Health, but the physician fees are so different in private or public hospitals and doctors’ offices

In this study, estimation of the asthma cost was carried out in a referral hospital and so the costs of physician visits and tests of respiratory rate were calculated by state current price, but if the patient had need to refer to private centers or doctor’s office for the mentioned routine tests, the costs go rise 2 or 3 times more than that of the amount paid in public hospitals

3. According to the second report from Strategic Committee of the International Plan for Evaluation of Prevalence of Childhood Asthma and Allergic Symptoms in children in 2004, the prevalence of asthma symptoms in Iranian children was estimated 13.2\% which showed an increase of 0.17%/year.\[^{[99]}\] In this regard, it is evident that the prevalence of asthma symptoms and in turn the average annual cost of asthma treatment has dramatically increased in recent years, which make significant economic burden for patients and their families.

Due to the fact that in our study, 49\% of total patient families and 36\% of patients families with severe asthma had an income below 407.88 it can be concluded that nearly half of the families of the patients participating in the study spend more than 10\% of monthly income on the treatment of asthmatic children.

In Iran, Asthma and Allergy Committee has been founded under the auspices of the National Committee of Non-communicable and Special Diseases in Ministry of Health. This committee implement the “National Plan of Asthma Control” in all aspects of research, education, health care, prevention, detection and treatment and determine the policies and solutions such as preparation booklets entitled “Prevention, diagnosis and treatment of asthma,” and holding conferences, seminars and congresses of presentation strategies to have control of asthma.

Since medication cost was the main driver of direct costs and travel costs constitute the main part of the direct non-medical costs, health policy makers must adequately support the implementation of “National Program of Control Asthma” by patient education in the base of self-management model to control disease, distributing 1 national asthma booklets among physicians, expanding insurance coverage for expensive inhalation drugs, launching specialized centers in different parts of the country for asthma treatment and employing specialized physicians, pharmacists and trained staff to control asthma resulting in a significant reduction in direct medical and non-medical costs. To achieve an effective treatment for diseases such as asthma, a multidimensional planning and operational strategies
should be created. In this regard, multiple methods of decision making, supporting and educational systems and broad commitment by the health care system are essential. For example, appropriate use of expensive corticosteroids, which incorporate prevention of inappropriate use or administration of these, are effective in reducing drug costs. These goals are obtained by proper physician education and encouraging them to use the guidelines in treatment.\textsuperscript{[31]}

This is the first study conducted to document the costs of the treatment of asthma in Iran. In summary, asthma not only disturbs patients’ lives and makes them so difficulties and suffering but also creates significant costs to health care system.

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.

\textbf{AUTHORS’ CONTRIBUTION}

All authors have contributed in design, experiments, manuscript preparation and final proofreading.

\textbf{REFERENCES}

1. Laforest L, Ernst P, Pietri G, Yin D, Pacheco Y, Bellon G, \textit{et al.} Asthma-related costs relative to severity and control in general practice. Pediatr Asthma Allergy Immunol 2005;18:36-45.

2. Rascati KL. Essentials of Pharmacoconomics. 1st ed. Philadelphia, PA: Lippincott William and Wilkins; 2009.

3. World Health Organization. The Global Burden of Disease: 2004 Update. Ginebra: World Health Organization; 2008. Available from: http://www.who.Int/evidence/bod. [Last accessed on 2012 Nov].

4. Fowler MG, Davenport MG, Garg R. School functioning of US children with asthma. Pediatrics 1992;90:939-44.

5. World Health Organization. Global surveillance, prevention and control of chronic respiratory diseases: A comprehensive approach, 2007. Available from: http://www.who.Int/evidence/bod. [Last Accessed: 2012 Nov].

6. Heidarnia MA, Entezari A, Moein M, Mehrabi Y, Pourpak Z. Prevalence of asthma symptom in Iran: A meta-analysis. Pjoujbesh 2007;31:217-25.

7. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Lancet 1998;351:1225-32.

8. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, \textit{et al.} Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. Lancet 2006;368:733-43.

9. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention 2007. Available from: http://www.ginasthma.org/. [Last accessed on 2012 Jul].

10. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention 2009. Available from: http://www.ginasthma.org/. [Last Accessed on 2012 Jul].

11. Nikfar S, Kebriaeezadeh A, Majdzadeh R, Abdollahi M. Monitoring of National Drug Policy (NDP) and its standardized indicators; conformity to decisions of the national drug selecting committee in Iran. BMC Int Health Hum Rights 2005;5:5.

12. Dinavand R. Iran: An evolving national drug policy. Essent Drugs Monit 1998;22:9-10.

13. Central Bank of the Islamic Republic of Iran 2013. Available from: http://www.cbi.ir. [Last Accessed on 2012 Sep].

14. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma (GINA) Program. The global burden of asthma: Executive summary of the GINA Dissemination Committee report. Allergy 2004;59:469-78.

15. Celik GE, Babvsek S, Paşaoğlu G, Mungan D, Abadoğlu O, Harmanci E, \textit{et al.} Direct medical cost of asthma in Ankara, Turkey. Respiratio 2004;71:587-93.

16. Blasco Bravo AJ, Pérez-Yarza EG, Lázaro y de Mercado P, Bonillo Perales A, Díaz Vazquez CA, Moreno Galdó A. Cost of childhood asthma in Spain: A cost evaluation model based on the prevalence. An Pediatr (Barc) 2011;74:145-53.

17. Bahadori K, Doyle-Waters MM, Marra C, Lynd L, Alasaly K, Swiston J, \textit{et al.} Economic burden of asthma: A systematic review. BMC Pulm Med 2009;9:24.

18. Barnes PJ, Jonsson B, Klim JB. The costs of asthma. Eur Respir J 1996;9:636-42.

19. WHO European Centre for Environment and Health. Effects of air pollution on children’s health and development - A review of the evidence. Copenhagen: WHO Region Office for Europe; 2005. Available from: http://www.euro.who.Int/document/E86575.pdf. [Last accessed on 2007 Mar 6].

20. Entezari A, Mehrabi Y, Varezvazirian M, Pourpak Z, Moin M. A systematic review of recent asthma symptom surveys in Iranian children. Chron Respir Dis 2009;6:109-14.

21. Sadatsafavi M, Lynd L, Marra C, Carleton B, Tan WC, Sullivan S, \textit{et al.} Direct health care costs associated with asthma in British Columbia. Can Respir J 2010;17:74-80.