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Original article

Clinical factors influencing asthma direct cost in children and adolescents with mild to moderate asthma

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Abstract

Asthma imposes a substantial economic burden on the health care system and community worldwide. Annual direct asthma cost and the factors that influence this cost are not yet addressed in Tunisia, particularly in the pediatric population. This study aimed to identify clinical factors determining the annual direct cost of pediatric asthma. The current study was cross-sectional, carried out in Farhat Hached University Hospital in Sousse, Tunisia, over three months among children with asthma aged 7-17 years. Asthma direct cost was defined as the cost of healthcare resources utilization and medication related to asthma in the past 12 months. Multiple regression was performed to examine the association between total asthma direct cost and clinical factors. Ninety children with mild to moderate asthma were included in the study. The findings showed that 67.8% were 7-11 years and 55.6% were boys. The annual mean of total direct asthma cost was $616.71±454. Multiple regression showed that severity of asthma (B1= 402.473, 95% CI 163.414 to 641.532, p=0.001), medication adherence (B2= -265.656, 95% CI -434.194 to -97.118, p=0.002), and quality of life of children (B3= -103.257, 95% CI -173.687 to -32.828, p=0.005) were significantly associated with asthma direct cost. In conclusion, this study underlined the substantial economic burden of mild to moderate asthma in Tunisian children and adolescents. Asthma direct cost increased with asthma severity stage, suboptimal medication adherence, and impaired quality of life. Asthma management action plans are needed to limit asthma direct cost.

Keywords: Asthma; Direct cost; Economics; Child; Adolescent; Tunisia.

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1. Introduction

Pediatric asthma is a common chronic disease worldwide [1]. It affects almost 14% of children, which makes it a potentially serious health problem in childhood causing disability-adjusted life years [1,2]. A high prevalence of asthma was noted among children in the age group ranging from 5 to 14 years with significant relevance in low to middle-income countries [3,4]. In Tunisia, it was estimated that the prevalence of asthma was 5.7% in male adolescents aged 10 to 15 years, and 5.6% in male children aged 5 to 9 years. The prevalence of asthma was more important in females with 6.4% in adolescents and 6.8% in children.

Childhood asthma had an enormous economic burden on families and the healthcare system. A recent study stated that the total adjusted asthma-related cost among adolescents with severe asthma was $5,112 per year in 2013 [5]. The same study reported that the adjusted asthma medication cost was $4,020 per year. Evidence showed that asthma exacerbation was associated with asthma medical costs. In their study, Puranitee et al. [6] examined the predictors of the direct medical cost of asthma care in children aged less than 20 years in Thailand. They found that asthma exacerbation at least once a year that requires hospitalization significantly increased the direct medical cost [6]. Determinants of asthma direct cost were largely investigated in adults with asthma. Zein et al. [7] revealed that the hospitalization cost increased with age, and it was higher in females. Sadatsafavi et al. [8] demonstrated that optimal asthma symptom control was associated with reduced asthma cost. Another study demonstrated that subsequent asthma cost was associated with asthma severity, smoking, and obesity especially in females [9].

To the best of our knowledge, the assessment of asthma direct cost and its associated factors in children with mild to moderate asthma was rarely explored. Mild and moderate asthma imposes a substantial burden on families and children. A recent study revealed that a sizeable number of children with mild asthma had uncontrolled asthma, a considerable risk of exacerbations, and suboptimal treatment adherence [10]. Another research conducted in children with mild to moderate asthma showed that the risk of acute health care use increased with asthma severity by 4.6-fold [11]. Furthermore, Jacob et al. [12] stated that frequent healthcare resource utilization increased healthcare costs. Therefore, it is interesting for pediatric nurses and policymakers to determine the direct cost of mild to moderate asthma and its

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associated factors in the pediatric population. This study aimed to determine the determinants of asthma direct cost in children with mild to moderate asthma.

2. Patients and Methods

Study design and setting

A cross-sectional study was carried out in children with asthma attending the outpatient clinic of pediatric pulmonology and allergology in a university hospital in Sousse for three months (April-June 2018). This hospital is the largest in the center of Tunisia that serves asthmatic children from different socioeconomic statuses, living in Sousse and neighboring cities. The pediatric pulmonology and allergology consultations were held each Wednesday of every week.

Inclusion and exclusion criteria

The age group of children ranged from 7 to 17 years with a confirmed asthma diagnosis at least 12 months before the study period, regardless of the stage of severity. Inclusion and exclusion criteria were described in a previously published article from the same work [11].

Data collection

Demographic and clinical data were recorded using a data collection sheet. Clinical information included asthma symptom control, asthma severity, quality of life, inhaler technique, medication adherence, asthma medication, and healthcare services utilization in the past 12 months (Emergency Department (ED) visit, hospitalization, asthma review visit, and general practitioner visit). Healthcare utilization data were parent-reported. The assessment of asthma symptom control and asthma severity was based on the Global Initiative for Asthma guidelines [13]. The clinical data collection instruments were fully described in a previously published article from the same work [14].

Direct costs were demonstrated by the costs of medication, hospitalization, ED, outpatient consultation, and general practitioner visits [14,15]. Drugs' costs and doses' numbers were recorded. To calculate medication cost, the number of drug-purchasing times in the past 12 months was multiplied by the drug's price in the same year. The cost of hospitalization was based on the number of hospital admissions in the past 12 months and the length of stay in each admission. The costs of ED visits, outpatient consultations, and general practitioner visits were estimated as follows: the number of visits in the past 12 months multiplied by the visit's price. The price of healthcare consultation or admission was identified from the health care pricing list from the Ministry of Health [16]. All estimated costs were quantified in Tunisian Dinars (TND). To enable international comparison, the purchasing-power-parity conversion factor in 2017 was used to convert TND to international Dollar (International $1= 0.704) [17].

Data analysis

Data were analyzed using the IBM SPSS statistics 20. The frequencies and percentages of dichotomous variables, and the means and standard deviations (SD) of continuous variables were reported. The normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Only healthcare use costs were not normally distributed. The association between the total direct cost related to asthma in the past 12 months and dichotomous predictive variables was performed using the independent T-test. Pearson's rank correlation was used to assess the association between asthma-related direct costs and continuous variables. Multiple regression analysis with the forward method was used to investigate factors independently influencing asthma-related direct costs, including all variables with a p-value <0.2 in the univariable analysis. All linear regression application requirements were verified. The regression model quality was verified. The significance level was set at $p<0.05$. The confidence interval was defined at 95%.

Ethical consideration

The scientific research ethics committee of the Faculty of Medicine approved this work under the reference number DEFMS 01/2018. The authorization of using the PAQLQ was obtained from Professor E.F. Juniper. Parents were given a letter explaining the study aim and the volunteer participation, following the Declaration of Helsinki II [18]. An informed consent form was signed by the parent. The assent of the child was considered. The recorded data was considered confidential and anonymous.

3. Results

Ninety subjects participated in this work. Table 1 shows that 53.4% of participants visited ED at least 1 time in the past 12 months, and 18.8% had at least 1 hospitalization in the past 12 months. Among our participants, 67.8% were boys and aged 7 to 11 years.

Table 2 reports the estimation of annual asthma direct cost in the past 12 months. The mean total asthma direct cost was $616.71±454. The highest expenditure was for asthma medication (72.56%, m=$447.54, SD=385.12). The annual median of healthcare utilization costs was equal to $100.142.

Predictors of annual asthma direct cost

Table 3 presents the results of univariable analysis. There was a significant difference between asthma direct cost and asthma severity ($p=0.004$), adherence to treatment ($p=0.007$), inhalation technique ($p=0.009$), and quality of life ($p=0.01$). Multiple regression analysis revealed that asthma severity ($\beta1=0.313$, $p=0.001$), controller adherence ($\beta2=-0.294$, $p=0.002$), and quality of life ($\beta3=-0.273$, $p=0.005$) predicted asthma direct cost in children with mild to moderate asthma (Table 4). Based on the final regression model presented in Table 4, the regression equation was:

Annual direct cost related to asthma = 1049.552 + 402.473 asthma severity - 265.656 controller adherence - 103.257 quality of life = 1083.112 USD.

4. Discussion

Recently, numerous published studies investigated the economic burden of asthma among adults [19–21]. However, the economic burden of pediatric asthma was less studied, especially mild and moderate asthma. This original study sought to estimate asthma direct cost and to identify its determinants in asthmatic children. This cost was higher than

Table 1. Demographic and clinical data of participants

Characteristics	n (%)
Age (years)	
7-11	61 (67.8)
12-17	29 (32.2)
Gender	
Male	50 (55.6)
Female	50 (44.4)
Health insurance	
Yes	31 (34.4)
No	59 (65.6)
Asthma severity	
Mild	77 (85.5)
Moderate	13 (14.5)
Asthma symptoms control	
Well-controlled	20 (22.2)
Partly controlled	46 (51.1)
Uncontrolled	24 (26.7)
Adherence to treatment	
Poor adherence	49 (54.4)
Good adherence	41 (45.6)
Inhaler technique	
Correct	41 (45.6)
Incorrect	49 (54.4)
Asthma medication	
Inhaled corticosteroids (Yes)	80 (88.9)
Anti-leukotrienes (Yes)	6 (6.7)
Short-Acting Beat agonists as needed (Yes)	60 (66.7)
Emergency department visits in the past 12 months	
None	42 (46.7)
1 visit	24 (26.7)
2 visits	10 (11.1)
≥ 3 visits	14 (15.6)
Hospitalizations in the past 12 months	
None	73 (81.1)
1 visit	12 (13.3)
2 visits	1 (1.1)
≥ 3 visits	4 (4.4)
General practitioner visits in the past 12 months	
None	73 (81.1)
1 visit	5 (5.6)
2 visits	4 (4.4)
≥ 3 visits	8 (8.9)
Asthma review visits in the past 12 months	
1 visit	1 (1.1)
2 visits	23 (25.6)
≥ 3 visits	66 (73.3)
Quality of life (PAQLQ), (m ± SD)	4.7 ± 1.2

The average annual direct cost related to pediatric asthma was approximately $616.71 for one child. Recently, numerous published studies investigated the economic burden of asthma among adults [19–21]. However, the economic burden of pediatric asthma was less studied, especially mild and moderate asthma. This original study sought to estimate asthma direct cost and to identify its determinants in asthmatic children. The average annual direct cost related to pediatric asthma was approximately $616.71 for one child.

Table 2. Estimation of asthma-related direct costs in children with mild to moderate asthma

Variables (USD)	m ± SD
Total costs	616.71 ± 454
Medications costs	447.54 ± 385.12
Healthcare utilization costs*	100.142 [0-942.47]

*median [minimum-maximum]

Table 3. Association between asthma-related total direct costs and participants' characteristics: Univariable analysis

Characteristics	Total Direct Costs m (SD)	p
Age (years)		
7-11	622.08 (490.95)	0.87
12-17	605.42 (372.11)	
Gender		
Male	562.40 (438.81)	0.2
Female	684.59 (468.98)	
Health insurance		
Yes	719.72 (476.04)	0.11
No	562.58 (436.37)	
Asthma severity		
Mild	560.23 (442.01)	0.004
Moderate	951.26 (386.85)	
Asthma symptoms control		
Well controlled	483.23 (277.77)	0.17
Partly controlled	610.57 (466.32)	
Uncontrolled	739.71 (526.35)	
Adherence to treatment		
Good adherence	752.16 (462.56)	0.007
Poor adherence	498.19 (415.84)	
Inhaler technique		
Correct	748.20 (463.51)	0.009
Incorrect	501.66 (417.05)	
	Pearson r	p
Quality of life (PAQLQ)	-0.025	0.01

the guaranteed minimum professional wage in 2017 ($485.34) [22]. The clinical factors determining asthma-related direct cost were the severity of the disease, the treatment adherence, and the quality of life of children.

In this study, the estimated pediatric asthma direct cost in Tunisia (lower-middle-income country) was high in comparison with upper-middle-income countries, such as Iran ($367.97±23.06) and Thailand ($278) [6,23]. This could be explained by the fact that 59% of the population in this study did not have health insurance, which can make the cost of asthma care high. Besides, the increase of health expenses in Tunisia was more dynamic than the economic growth [24]. Hence, households financed more than half of health expenditure, which can explain the current findings.

Since 2011, the funding of the Tunisian health care system has been characterized by three dangerous facts that threaten its performance: an excessive expenditure compared to the country's growth, a very high contribution from households exceeding the threshold of expenses, and a marked drift in the social policy of the National Sickness Insurance Fund "CNAM", to the benefit of the private sector [25]. The present data corroborated these facts. Similarly, the national cost of asthma among children in the United States was high ($847) in comparison with the mentioned studies [26].

Although 85.5% of children had mild asthma, the highest cost belonged to asthma medication. Several studies confirmed that medication usually had the highest cost [12,23,26]. This study revealed that asthma direct cost significantly increased with the severity stage of asthma, suboptimal medication adherence, and poor quality of life. The predictors identified in the literature were controversial. Sharifi et al. [23] found that total asthma cost in children was significantly associated with asthma control status. The same study reported that total asthma cost was higher in boys than girls, and in children aged 7 to 11 years than those aged less than 7 years. Puranitee et al. [6] demonstrated that having at

least one asthma exacerbation raised the annual asthma direct cost, especially exacerbation requiring hospitalization. Nonetheless, this study did not report a significant association of asthma direct cost with asthma control, age, gender, and exacerbation. In another paper, researchers found that asthma symptoms control, acute health care utilization due to asthma exacerbation, and gender were significantly associated with the quality of life of children with asthma [11]. These data suggested that the named factors impaired the quality of life of children and indirectly increased direct asthma cost. Furthermore, the Global Initiative for Asthma stated that treatment issues, such as poor treatment adherence, are risk factors for future asthma exacerbations [13]. This fact might explain the negative and significant association between asthma direct cost and treatment adherence in this study.

Numerous limitations of this study should be mentioned. First, the absence of a control group of children without asthma was disadvantageous in demonstrating the economic burden of asthma. Besides, the sample size was limited, which makes the current findings are not generalizable. Also, there is a high risk of selection bias due to the homogeneity and the non-representativity of the sample. Nevertheless, clinical-based studies have greater certainty and provide real-world cost estimation. Healthcare utilization was parent-reported, which can produce a memorization bias. However, since healthcare services use is a critical life event, parent-report could be relevant. Cross-sectional studies were always associated with a risk of information bias. Therefore, cohort studies should be conducted to accurately report annual asthma costs.

Table 4. Multiple regression analysis: Predictors of asthma-related direct costs in children with mild to moderate asthma

Predictors	B [95% CI]	SE	β	p
Constant	1049.552 [539.625 to 1559.479]	256.511		10^{-3}
Asthma Severity	402.473 [163.414 to 641.532]	120.255	0.313	0.001
Controller adherence	-265.656 [-434.194 to -97.118]	84.780	-0.294	0.002
PAQLQ	-103.257 [-173.687 to -32.828]	35.429	-0.273	0.005
R^2adjusted = 0.22				
F = 9.38				10^{-3}

This study adds to existent literature that mild and moderate asthma had a significant economic burden associated with the severity of the disease, medication adherence, and quality of life of affected children. To the best of our knowledge, this was the first work that explored the cost of mild to moderate pediatric asthma. These results are challenging for the healthcare system and sickness insurance funds. Based on these data, the funding of the Tunisian healthcare system should be revised to reduce the excessive expenses supported by the households. Besides, establishing healthcare insurance plans in favor of patients and the public sector is crucial to limit the economic burden of asthma on households and the healthcare system. Enhancing the quality of life of children and medication adherence through asthma management action plans is potentially essential in achieving optimal asthma control and reducing direct asthma costs. This study can be useful for local physicians and policy makers. Further studies with larger samples are required to estimate the national economic burden of asthma. These studies are also needed for the assessment of the effectiveness of public healthcare policies.

In conclusion, this study highlighted the substantial economic burden of mild to moderate asthma in Tunisian children. The average annual direct cost related to asthma was $616.71, higher than the guaranteed minimum professional wage in the same year. The highest expenditure was for asthma medication. The annual asthma direct cost was significantly and independently associated with the severity of asthma, medication adherence, and quality of life of children. These findings underlined the urgent need for a national asthma management plan to limit the economic burden of asthma. Considering the lack of sickness insurance funds and the excessive health care expenses, asthma management programs could be a suitable solution to reduce the burden of the disease.

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Conflict of interest disclosures

The authors declare no competing interest.

Authors' contributions

Conception and design: MD, JB; Acquisition of data: MD, JB; Data analysis: MM, JS, MD; Interpretation of data: JS, MM; Drafting the article: MD; Critical revision of the article: CZ, AM; Final approval: all authors.

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