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Risk factors hindering asthma symptoms control in Saudi children and adolescents.

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Short title: Lack of asthma education, medication compliance and inappropriate device use.

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Abstract

Background: Maintaining well control of asthma symptoms can help preventing exacerbations and its associated complications. The Asthma Control Test (ACT) can rapidly assess the effectiveness of asthma management plan and therapy.

Objective: To identify risk factors associated with uncontrolled asthma symptoms in young Saudi asthmatics (3-17 years-old).

Methods: In this cross-sectional hospital-based survey, the ACT was administered to 297 asthmatic children/adolescents, recruited at the emergency department (ED) of two major hospitals.

Results: Most recruited patients were intermittent (63.5%) and mild-persistent (27.6%) asthmatics; few were moderate-persistent (8.9%) and none were severe asthmatics. These patients visited the ED 4 times (3.9 ± 3.2), on average. Almost half of patients declared not receiving education about asthma (47%) nor education about medication use (43%). Most patients (60.3%) had uncontrolled symptoms (ACT score ≤ 19), of which intermittent asthmatics presented better scores than patients with more severe symptoms. Children ≤ 6 years-old, with symptoms diagnosed < 5 years ago and who were not attending school, had significantly worse control than older patients. Poor medication compliance and inappropriate inhaler device use were ascribed to younger patients (< 12 years-old) and worse scores; particularly in relation to the practice to stop inhaled corticosteroid (ICS) therapy when their

symptoms improve. Patients with poor control declared also not having received education about inhaler device use.

Conclusions: Most Saudi asthmatic children/adolescents visiting the ED had poor control of symptoms; indeed, none achieved complete control, which is related to deficient medication compliance and improper medication inhaler device use; deficient knowledge about asthma was also another factor hindering control.

Key words. Pediatric asthma; asthma control test; risk factors; Saudi Arabia; medication compliance; inhaler device; MDI; DPI.

Introduction

The current definition of control of asthma symptoms was recently discussed by a multi-member task team that included members of the American Thoracic Society (ATS), The Food and Drug Administration (FDA), the European Medicines Evaluation Authority (EMA) and various representatives from major respiratory pharmaceutical companies.^[1] By consensus, this team proposed that Asthma control be defined “as the extent to which the various manifestations of asthma have been reduced or removed by treatment”.^[1] This concept has proven useful for clinicians who need to evaluate reliably the current state of a patient's symptoms relative to a previous status, and to conclude unambiguously whether a current management strategy/therapy is being effective at improving the general well being of the patient.

The goal pursued by the clinician and the patient is to achieve complete control of symptoms.^[2,3] Although control of symptoms is determined in great extent by the effort put by the patient at following precisely the management plan discussed with the

clinician/generalist and by regular follow up, it is the latter who needs to assert quickly and as precisely as possible, the status of the patient during the short patient's visit; the outcome of that evaluation should be useful in the decision to modify or to maintain the current therapy plan.

Toward this goal, a number of assessment tools have been developed, which are based on different measurements such as physiological parameters, biomarkers, severity of symptoms, and patient-based surveys.^[2,4,5] One of the most frequently applied tests is the Asthma Control Test (ACT), which has the advantages of being short, easy-to use and reliably measures asthma control.^[6] The ACT aims to assess directly the status of the patient through a series of questions about present symptoms, within a relatively short period of time, hence compatible with the clinicians' busy schedule.^[6,7] The ACT test has been validated in a number of studies;^[8-11] furthermore, this tests was found to correlate better with the rating by the asthma specialist than with FEV1 values in determining the patient's asthma control.^[6,11]

In Saudi Arabia, approximately two million people suffers from this disease; in particular, 8-23% of school students are asthmatic, depending on the region, indicating that a majority of asthmatic patients is composed of children and adolescents.^[12-14] To our knowledge, only one survey study has been done recently using the ACT test in asthmatic Saudi children, and found that several socioeconomic factors, including family income, household crowding, and the number of siblings were associated with asthma control issues.^[15] Therefore, in this study, we applied a validated Arabic version of the Asthma Control Test questionnaire (ACT) to further the analysis of ACT scores in a group of Saudi asthmatic children.^[11,16] The objective of this study was to identify major risk factors (demographic, clinical, knowledge about asthma disease and medication use) associated with poor control of symptoms in asthmatic children from Saudi Arabia.

Methods

Recruitment of patients

In this cross-sectional study, 297 physician-diagnosed asthmatic children and adolescents of ages between 3 and 17 years old were randomly recruited at the time of their visit to the emergency department (ED) for asthma-related causes. Recruitment was done during a period spanning 14 months at two major care facility centers: the King Saud University-King Khalid University Hospital and the King Abdulaziz medical city, in Riyadh, Saudi Arabia. The Ethics Committees of both hospitals approved the study. All caregivers were able to read and write, and a written signed consent was obtained from the caregiver accompanying the patient at the time visiting the ED. The criteria for inclusion were as follows: a) age group between ≥ 3 years and < 18 years old; b) confirmed diagnosis of asthma made by the primary care physician, and classified by severity according to GINA guidelines;^[2,3] c) the child/adolescent should have previously frequented the ED because of an acute asthma exacerbation. Patients having other co-morbidities diagnosed by a physician, including congenital lung diseases, cystic fibrosis, or airway infections were excluded.

Data collection

The validated Arabic version of the Asthma Control Test questionnaire (ACT) was administered to determine the control of symptoms of each patient.^[6,11] For each question, a trained interviewer asked the accompanying caregiver to select the best answer from a set of five scored options: scores ranged from 1 (not controlled) to 5 (best controlled). Each test question explores different aspects of control: 1) In the past 4 weeks, how much of the time did your asthma kept you from getting as much done at school or at home? 2) During the past four weeks, how often have you had shortness of breath? 3) During the past four weeks, how often did your asthma symptoms (wheezing, cough, shortness of breath, chest tightness, or

pain) woke you up at night or early in the morning? 4) During the past four weeks, how often you have used your rescuer medication (inhaled or nebulized) such as albuterol? 5) During the past four weeks, how would you rate your asthma control? The total sum of scores was calculated (by summing up the scores of the five-question tests), which ranged from 5 (worst controlled) to 25 (completely controlled). The interviewer also collected information about demographic (e.g., age, gender, schooling level, etc), and clinically-related aspects, such as the use and frequency of medication for asthma therapy, whether the patient received education about bronchial asthma as a disease, or education about the use of inhaler devices. The patient/caregiver were tested to determine the proper use of the prescribed medication inhaler device. The caregiver also provided information on the number of visits to the ED and hospitalizations during the year prior to interview.

Statistical analysis

The minimal sample size, n , was calculated using Cochran's formula: $n = Z^2pq/d^2$, where Z is the standard deviation at 95% CI (1.96); p is asthma's prevalence (prevalence of asthma has been estimated at 8-23% in Saudi Arabia;^[12-14] therefore, we used the highest value reported, 23%, for better representation); q is the difference ($q = 1 - p = 1 - 0.23 = 0.77$); and d is the accuracy level (0.05). The calculated minimum sample size was 272, for an actual hospital-based recruited number of 297 patients. All analyses were performed using the GNU PSPP software package version 0.8 (Free software Foundation), or the Prism software version 5 (GraphPad). Descriptive analyses of the clinical and demographics data were performed, such as means, medians, standard deviations and percentages. ACT scores per question and total sum of scores were analyzed by independent T tests and ANOVA; for variables with multiple groups, Bonferroni multiple comparison tests were performed. Chi-square tests of independence were performed to test the association of the dichotomous variables clinical,

demographic and the factors explored. A logistic regression model was built to assess the association of poor asthma control (ACT score ≤ 15) with predictors pertaining to clinical, demographical and education about asthma and medication use, by using a forward selection method. Significance was considered at two-tailed $P < 0.05$.

Results

Clinical description of the recruited asthmatic children and adolescents

Principal clinical and demographic characteristics of the 297 asthmatic children and adolescents recruited are presented in Table 1. The mean age was 8.1 years old, with a standard deviation of ± 5.5 . The male/female ratio was 2.0. A majority of children (45.9%) was not attending to any school at the time of the interview; and most of these illiterate children (82.5%) were 5 years old or younger; reportedly, only about 10% of Saudis take their children to a kindergarten, since it is not mandatory for enrollment to first grade of primary education (World Data on Education, UNESCO, 2010/2011). Most of the patients were diagnosed as intermittent (63.5%) and mild-persistent (27.6%); there were few moderate-persistent patients (8.9%), whereas severe persistent asthmatics were absent. The mean duration of asthma diagnosis was 5.3 ± 4.8 years at the time of the interview. These patients visited the ED nearly 4 times per year (3.9 ± 3.2), on average; most of them (61.6%) made more than 3 visits per year, whereas 38% made less than 3 visits. Visits to the outpatient clinic (2.6 ± 3.0 visits per year) or hospital admissions (1.2 ± 2.2 visits per year) were less frequent than the ED. The ACT scores over the last month indicated that the majority of the cohort (60.3%) had their asthma symptoms uncontrolled (ACT score ≤ 19), whereas the remaining 39.7% had partially controlled symptoms (score $\geq 20 \leq 24$); none of the patients achieved complete control (score =25). Fifty three percent of patients declared receiving some education about asthma disease and 47% did not. A slight majority of patients

(57%) acknowledged receiving education about medication use. The use of inhaled corticosteroid (ICS) and frequency were requested: 56% patients were using ICS, of which more than half (56.1%) reported using it daily, twice per day. The ICS was used mainly at low (41.9%) and medium doses (43.4%), whereas only 2.2% of patients were taking a high dose. Flixotide (Fluticasone propionate) was the most frequently mentioned ICS (37.7%); Rhinocort (Budesonide) and Nasonex (Mometasone) were used to treat nasal polyps and allergic rhinitis; Ventolin (Salbutamol), Symbicort (Budesonide + Formoterol), and Seretide (Fluticasone + Salmeterol) were also frequently mentioned (Table 1, legend). Some patients were prescribed more than one medication; the use of a bronchodilator (Salbutamol) was reported by most patients (92.5%), either as only therapy (51.1%) or as rescue therapy daily (35.6%). Singulair (Montelukast sodium) was the only leukotriene inhibitor in use by almost half of them (46.6%). The metered-dose inhaler (MDI) was the device used the least (18.3%), whereas the dry- powder inhaler (DPI) and the nebulizer were the most frequently reported devices for medication administration (36.9% and 44.9%, respectively).

Influence of demographic and clinical factors on uncontrolled asthma symptoms

To identify demographic and clinical factors linked to poor asthma control, the ACT sums of scores were analyzed by independent T tests (dichotomous variables) and by Bonferroni multiple comparison tests (for variables with multiple groups) (Table 2). Several demographic factors including age, school attendance and schooling levels significantly influenced ACT scores, indicating that patients ≥ 12 years old, who attended school, particularly secondary and high-school level, had significantly higher scores (better control) than those of younger age (< 6 years old) and who were not attending any school.

Gender did not significantly influence ACT score. In the case of clinical variables, both the duration of disease since diagnosis and the severity of asthma symptoms did influence

significantly asthma control scores: patients who were diagnosed with asthma for a period of ≥ 5 years presented better control of symptoms than those with < 5 years since diagnosis of asthma. Also, mild persistent and moderate persistent asthma patients had significantly lower scores (poor control) than intermittent asthmatics. Frequency of visits to the ED did not affect significantly ACT scores.

Chi-square tests suggested a relationship between age and some aspects of medication adherence and appropriateness in the use of the inhaler device (Table 3): younger patients (< 12 years old) had greater odds of having asthma symptoms during a period < 5 years since diagnosis (OR=28.7; 95%CI=13.9-60.3; $P < 0.0001^*$), and were more likely of being afflicted with moderate persistent asthma (OR=4.5; 95%CI=1.2-19.6; $P = 0.01^*$); also, odds were greater for these younger children to wrongly use their medication, such as to initiate or increase ICS therapy when an attack is perceived (OR=2.8; 95%CI=1.6-4.9; $P < 0.0001^*$); or not initiating bronchodilator therapy when an attack is perceived (OR=4.0; 95%CI=1.8-8.9; $P < 0.0001^*$), and were more likely of using inappropriately an inhaler device (OR=1.95; 95%CI=1.1-3.6; $P < 0.0001^*$), comparatively to older patients (≥ 12 years old (Table 3).

Influence of medication compliance and knowledge on medication device use on uncontrolled asthma symptoms

Table 4 shows the relationship of asthma control test scores with variables pertaining to the patient's knowledge about medication and utilization of devices. In this analysis, six of the 9 variables explored did influence significantly asthma control scores. Specifically, patients who stop ICS medication when their symptoms improve had significantly worse score (17.10 ± 0.28) than those who do not stop medication (18.48 ± 0.32 ; $P = 0.01$). Likewise, patients who increase or initiate ICS use when an attack is perceived showed worse control (15.8 ± 0.42)

than those who do not (18.41 ± 0.24). Patients who confirmed to initiate or increase bronchodilator medication when an attack is perceived had also worse control of symptoms (17.15 ± 0.27), relative to those who were using it regularly (18.45 ± 0.39). Another important factor identified that significantly influenced control scores was the type of device used for medication delivery: worst control (14.55 ± 0.43) was observed in patients who reported using a MDI, whereas those who used a nebulizer or a PDI had better control scores (17.67 ± 0.37 and 19.27 ± 0.26 , respectively). Furthermore, those patients who declared having received education about inhaler device use had significantly better control scores (18.01 ± 0.27), comparatively to those who did not (16.71 ± 0.38); this relationship is supported by the finding that patients using appropriately the inhaler device had significant better scores than those who used it inappropriately (18.1 ± 0.25 and 16.0 ± 0.5 , respectively; $p < 0.05$).

Influence of education on asthma management on uncontrolled asthma symptoms

Table 5 shows the relationship of asthma control scores with variables pertaining to the patient's education about asthma as a disease. Patients/caregiver who declared to have discussed a prospective plan on how to manage asthma symptoms with the physician had significantly better scores than those who have not (total sums scores 18.08 and 17.01, respectively; $P = 0.02$). Other variables analyzed had no significant effect on control score, although significance for some item questions was observed when they were analyzed individually.

A logistic regression model was calculated to further understand the association of asthma control scores with demographic, clinical and other predictors. In this model, patients were divided in two groups by ACT scores: those with scores ≤ 15 correspond to 'poor controlled symptoms' group, as proposed by Nathan et al. (2004) (Table 6).^[6] Of the six significant

variables in this model, all had positive coefficients except for 'Presence of environmental triggers'; positive coefficients indicate an increase in the log odds of poor control. The following variables were positively associated with poor control: The patient 'increases or initiates steroid therapy when an attack is perceived' (OR=4.78); with asthma diagnosed <5 years (OR=5.47); has moderate persistent asthma (OR=3.34); uses the bronchodilator (SABA) in multiple ways (OR=1.51); and has not 'discussed a prospective plan on how to manage asthma with the physician' (OR=2.91).

Discussion

In Saudi Arabia, where the majority of asthmatic patients are under 18 years old,^[14,17] few studies have been dedicated to understand the factors leading to poor control of symptoms in this subgroup; therefore, physicians and pulmonologists are in great need of information in this topic. In this study, we identified several factors that significantly influenced control of symptoms outcome, principally, in relation to non-compliance to medication, lack of education and inappropriate medication device use. Of these factors, education about medication use and proper use of the medication delivery device were of special concern. The problem of lack of adherence to the guidelines on long-term medication has been reported in several societies,^[10,18,19] and we could confirm that it is also the case in asthmatic children/adolescents from Saudi Arabia. Non-compliance on the long-term use of medication was observed in wrong practices such as stopping their medication (ICS) as soon as their symptoms improve, and by increasing or initiating ICS when an attack is perceived; in addition, a significant risk on the over-use/under-use of the bronchodilator was also uncovered. Regarding the medication delivery device, this study revealed an important influence of the lack of knowledge on the proper use of the inhaler device, resulting in significantly lower control scores. Importantly, the worst control scores were observed in

children using a metered-dose inhaler (MDI), whereas users of a dry- powder inhaler (DPI) presented the best scores, followed by the nebulizer. Moreover, most adolescents (>12 years old; 90%) were using a DPI, and few (6%) were using a MDI while having globally better control of symptoms; in contrast, younger children (<12 years old) presented worse control scores, and were using mostly a nebulizer (68%) or a MDI (26%), but few were using a DPI (6%). The implemented Medical practice followed the guidelines to use MDI with aerochamber for young children below 7 years, and older children who can not use the DPI properly. The reason why worst control scores were seen in children using MDI is most likely attributed to the improper use of the technique, or using without aerochamber despite for the prescription. Another reason that should not be excluded could be the improper education about the technique and especially the importance of using the aerochamber with the MDI. In this respect, a recent analysis of data from the Cochrane Central Register of Controlled Trials, concluded that nebulizers could be more effective than MDI devices at administering bronchodilators in adults.^[20] Furthermore, it was reported recently that an elevated proportion of Saudi asthmatic adults showed improper use of the inhaler device, which was associated with uncontrolled symptoms.^[21] Also, in younger children, technical difficulties and lack of training on the use of the MDI may be associated with defective medication delivery.^[22]

On the other hand, this study also discloses the significant importance of knowledge of asthma as a disease in asthma control. Patients with lack of knowledge, such as that the caregiver/patient had not discussed with their physician a prospective plan on how to manage asthma symptoms, had greater odds of worst control. This observation is consistent with the fact that the majority of the caregivers admitted not having received education about asthma disease (53%). Of note, various other aspects of education about asthma analyzed, failed to significantly influence control (as sum of scores); however, using an alternative analysis by

individual test, we could confirm significant effects by aspects that include not having discussed a prospective plan on how to manage asthma with the physician, and not having discussed ways on how to prevent, or how to treat mild and severe symptoms with a physician.

In relation to clinical and demographical factors, we could confirm that patients diagnosed with moderate-persistent asthma had worst scores than those patients with milder disease (intermittent and mild-persistent); a significant effect of the severity of disease on control scores has been also reported by others.^[23] In this regard, it is well known that even with consistent use of ICS, a significant proportion of children and adolescents cannot achieve well controlled symptoms, suggesting that other factors are involved.^[24] Therefore, particular attention should be dedicated to patients with more severe disease. This study also revealed that younger children (<12 years old) who attend Primary school or none, have the worst control of symptoms in relation to older patients ($\geq 12 < 18$ years old) who attend Secondary school or higher level. In congruency with the above, younger children were characterized for having their symptoms diagnosed less than 5 years ago, and were more likely to have moderate-persistent and mild-persistent symptoms. These observations are in good agreement with a recent report on a cohort of 247 young Saudi asthmatic children (4 to 11 years old) indicating that the majority of patients (59.3%) had their symptoms uncontrolled.^[15] In contrast, we found that the majority of adolescents ($\geq 12 < 18$ years old) had intermittent-persistent symptoms, which were diagnosed more than 5 years ago (66% and 73%, respectively). Therefore, these findings underline the need of physicians in general and pulmonologists in particular, to take special care and attention of younger patients who are in greater risk of uncontrolled symptoms and exacerbations, to further improve ways to effectively prevent morbidity.

Strengths and limitations

The strength points of this study are the large cohort (297) of asthmatic children and adolescents 3 to 17 years old, with confirmed diagnosis by a physician and medical records; the direct interviewing of the caregiver with sets of questions exploring their knowledge about asthma and medication use; the confirmation of clinical and demographic data from medical records. A major limitation is that we did not collect information regarding parent's academic formation, education about asthma, nor economic status, variables that potentially have an impact and should be addressed in future studies. Nevertheless, we recently published data from a cohort of Saudi asthmatic children, in which lack of education about asthma and non-compliance in medication were two major factors associated with asthma attack and with increased number of visits to the emergency department.^[26] Regarding economic status, a recent study reported that income households <15 000 Saudi Riyal increased the odds of having uncontrolled asthma by 2.30 (95% CI= 1.02-5.21).^[15] Also, we did not make pulmonary function tests. However, lung test function parameters such as FEV1, with their fluctuations over time, do not always correlate with the perception of the disease by the patient, as measured with a questionnaire,^[7,18] seemingly, lung function tests are good at measuring aspects of asthma inflammation/hyper-responsiveness but less sensitive at assessing control.^[12,25] Another possible limitation is that we applied the ACT to both adolescents and children under 11 years old; this decision was based on the goal to keep a uniform score range for valid comparisons and statistical analyses; even though we made sure that children were assisted by their caregiver whenever he/she needed help at reading or understanding the question and provide an answer, the childhood ACT would be more suitable for literate children under 11 years old. Also, the ACT questionnaire is limited in that it measures control of symptoms within a recent short term (past 4 weeks).^[6] In addition, we could not recruit severe-persistent asthmatics; although this could be interpreted a priori as

biased sampling, it should be noted that recruitment was done in random fashion and spanning a period of 14 months; this may suggest that very few children of that category were visiting the ED. Future studies should consider the recruitment of more patients in a larger cohort study that addresses the above limitations.

Conclusion

Considering that none of the patients succeeded in controlling completely their symptoms (score of 25), our study uncovers potential flaws or deficiencies in the current state of the Saudi asthma management system, by not achieving the GINA goals.^[2,3] Efforts should be invested towards the improvement of communication between the caregiver and the physician, to monitor regularly their asthma control of symptoms, and to ensure that the patient/caregiver receives adequate education in both asthma and use of medication. In this regard, several reports demonstrated that improvement of asthma control can be obtained by providing the appropriate information to the patient in order to understand their disease, the appropriate use of medication and inhaler devices.^[27-29]

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Conflicts of Interest: The authors declare to have no conflicts of interest regarding this study.

Contributors list: N. Horanieh, S. Dulgom, Z. Al-Aseri, N. Al-Khamis, and Z. Al-Sum were responsible for the recruitment, and interviewing of patients and subjects, and data collection. R. Halwani and A. Vazquez-Tello organized and compiled the data, performed the statistical analyses and wrote the manuscript. S. Al-Muhsen, and H. Al-Jahdali participated in the initial phase of planning and design of the study, and analyzed the clinical history of the recruited patients.

Statement: All authors acknowledge having read and approved this manuscript, and believe that all the information contained within represents honest work. All authors have met the requirements for authorship.

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Table 1. Principal demographic and clinical information of the asthmatic children.

Variable	Level	Value
Age (in years)	Mean $\pm$ Sdev	8.1 $\pm$ 5.5
Gender	Male	194 (66.9%)
	Female	96 (33.1%)
Schooling attendance/age range	[§] Pre-school ≤ 5 years old	124 (45.9%)
	Primary 6-12 y. o.	56 (20.7%)
	Secondary 13-15 y. o.	72 (26.7%)
	High School ≥ 16 y. o.	18 (6.7%)
Frequency of ED visits (per year)	Mean $\pm$ Sdev (Median; range)	3.9 $\pm$ 3.2 (3; 0-22)
	Patients with < 3 visits to ED	76 (38.4%)
	Patients with ≥ 3 visits to ED	122 (61.6%)
Frequency of Outpatient clinic visits (per year)	Mean $\pm$ Sdev (Median; range)	2.6 $\pm$ 3.0 (2; 0-20)
Frequency of hospital admissions (per year)	Mean $\pm$ Sdev (Median; range)	1.2 $\pm$ 2.2 (0; 0-15)
Asthma duration (in years)	Mean $\pm$ Sdev	5.3 $\pm$ 4.8
Classification of asthma severity	Intermittent	186 (63.5%)
	Mild-persistent	81 (27.6%)
	Moderate-persistent	26 (8.9%)
	Severe-persistent	0 (0.0%)
¹ ACT control level of symptoms	*Total sum of scores	17.4 $\pm$ 3.6
	Poorly controlled (≤ 15)	77 (30.5%)
	[#] Uncontrolled (≤ 19)	152 (60.3%)
	Partially controlled (20-24)	100 (39.7%)
	Controlled (25)	0 (0.0%)
Received education about asthma disease?	Yes/No	154 (53%) / 137 (47%)
Received education about medication use?	Yes/No	168 (57%) / 125 (43%)
² Use of inhaled corticosteroids	Yes/No	164 (56%) / 129 (44%)
	If Yes, how often:	
	Once per day	8.1%
	Twice per day	56.1%
³ Use of a bronchodilator (SABA)	When symptomatic only	35.8%
	Yes/No	272 (92.5%) / 22 (7.5%)
	*Number of puffs per day?	3.3 $\pm$ 2.2
Way of using the bronchodilator	As only therapy	135 (51.1%)
	As rescue therapy, daily	94 (35.6%)
	As rescue therapy, once/week	1 (0.4%)
	Several options	34 (12.9%)
⁴ Use of leukotriene receptor antagonist	Yes / No	138 46.6%) / 159 (53.4%)
Device used for medication delivery	Nebulizer	118 (44.9%)
	Dry-powder inhaler	97 (36.9%)
	Metered-dose inhaler	48 (18.3%)

[§]Pre-school children: none of them were attending a kindergarten nor a day care facility. ¹ACT total sum of scores ranged from 5 (not controlled) to 25 (completely controlled) (Nathan et al. 2004). [#]The Uncontrolled group consist of all patients with ACT ≤ 19 including the poorly controlled group. ²Most frequently reported medicines: Flixotide (Fluticasone), 37.7%; Simbicort (Budesonide + Formoterol), 29.0%; Seretide (Fluticasone + Salmeterol), 16.7%; Rhinocort (Budesonide), 24.6%; Nasonex (Mometasone), 8%. Patients taking a low ICS dose: 41.9%; medium ICS dose: 43.4%; high ICS dose: 2.2%. ³Ventolin (Salbutamol). Equivalent amounts of Ventolin inhaler: one puff delivers 100 micrograms (μg) of Salbutamol. ⁴Montelukast (Singulair).

Table 2. Association analysis of ACT scores with demographic and clinical factors.

	Variables	Groups	Score $\pm$ SE	P values
Demographic	[†] Gender	Males	17.71 $\pm$ 0.27	0.22
		Females	17.13 $\pm$ 0.4	
	[‡] Age	<6 years old	16.59 $\pm$ 0.35	>0.05
		≥ 6 to <12 y.o.	16.27 $\pm$ 0.5	
		≥ 12 y.o.	19.44 $\pm$ 0.26	
	[†] School attendance	No	16.79 $\pm$ 0.37	<0.01*
		Yes	18.77 $\pm$ 0.25	
	[‡] Schooling levels	[§] Pre-school	16.79 $\pm$ 0.37	>0.05
		Primary	18.32 $\pm$ 0.46	
		Secondary	19.03 $\pm$ 0.33	
		High-School	19.44 $\pm$ 0.42	
Clinical	[†] Duration of disease	<5 years	16.93 $\pm$ 0.3	<0.01*
		≥ 5 years	18.24 $\pm$ 0.33	
	[‡] Severity of Asthma	Intermittent	18.35 $\pm$ 0.27	<0.01*
		Mild Persistent	16.74 $\pm$ 0.37	
		Moderate Persistent	13.88 $\pm$ 0.65	
	[†] ED visits	<3 times per year	17.01 $\pm$ 0.45	0.27
		≥ 3 times per year	16.37 $\pm$ 0.37	

[§]Pre-school children: none of them were attending a kindergarten nor a day care facility. [†]Independent-samples T tests. [‡]Bonferroni multiple comparison tests; 'Pre-school' was compared to other schooling groups; <6 years old group was compared to other age groups; 'Intermittent' was compared to other asthma groups. *Significant differences between groups, at two-tailed P<0.05.

Table 3. Odds ratios and 95% confidence intervals for younger patients (≤12 years old) in relation to risk factors.

Risk factors	[‡] Levels	Age		X ²	[†] OR (95% CI)	[*] P values
		<12 years old	≥12 years old			
Duration of asthma symptoms	≤5 years	151	33	122.7	28.7 (13.9-60.3)	<0.0001*
	>5 years	14	88			
Severity of asthma	Moderate persistent	22	3	6.5	4.5 (1.2-19.6)	0.01*
	Mild persistent	49	32	0.01	0.9 (0.5-1.7)	0.89
	Intermittent	111	68			
Initiate or increase ICS	Yes	86	25	14.3	2.8 (1.6-4.9)	<0.0001*
	No	97	78			
Initiate or increase bronchodilator	No	55	10	15.7	4.0 (1.8-8.9)	<0.0001*
	Yes	127	93			
Received education about medication device use	No	81	38	1.4	1.3 (0.8-2.3)	0.26
	Yes	101	64			
Inhaler device use is appropriate	No	56	21	5.2	1.95 (1.1-3.6)	0.026*
	Yes	108	79			
Type of medication device used	MDI	41	6	77	59 (18-204)	<0.0001*
	Nebulizer	110	3	156	315 (76-1538)	<0.0001*
	DPI	10	86			

[†] For each dichotomous factor, odds ratios and 95% confidence intervals were calculated for the risk level (upper)[‡]. *Significance was considered at two-tailed P <0.05.

Table 4. Relationship of ACT scores with risk factors pertaining to education about medication and inhaler device use.

Variables	Groups †	Score ±SE	P values
Believes that asthma medicines are unsafe	Yes	17.52 ±0.42	0.82
	No	17.42 ±0.27	
Believes that asthma medicines are addictive	Yes	17.28 ±0.45	0.66
	No	17.51 ±0.27	
Believes that asthma medicines may lose effectiveness	Yes	18.07 ±0.4	0.06
	No	17.15 ±0.28	
Stops medication when symptoms get better	Yes	17.10 ±0.28	0.01*
	No	18.48 ±0.32	
Increases or initiates ICS when an attack is perceived	Yes	15.80 ±0.42	<0.01*
	No	18.41 ±0.24	
Increases or initiates bronchodilator when an attack is perceived	Yes	17.15 ±0.27	0.02*
	No	18.45 ±0.39	
Received any education about medication device use	Yes	18.01 ±0.27	<0.01*
	No	16.71 ±0.38	
‡ Medication is delivered with:	DPI	19.27 ±0.26	<0.001*
	Nebulizer	17.67 ±0.37	<0.001*
	MDI	14.55 ±0.43	
Inhaler device use is appropriate	Yes	18.1 ±0.25	<0.01*
	No	16.0 ±0.51	

† Independent-samples T tests (Yes vs. No groups). ‡ Bonferroni multiple comparison test: 'Metered-dose inhaler' is compared to the other delivery devices. * indicates significant differences between groups at two-tailed P<0.05.

Table 5. Relationship of ACT scores with factors pertaining to education about asthma disease.

Variables	Groups †	Scores ±SE	P values
Regular medical checkups for asthma	Yes	17.66 ±0.26	0.18
	No	17.01 ±0.44	
Received any education about bronchial asthma	Yes	17.85 ±0.29	0.06
	No	17.0 ±0.36	
Knows what triggers asthma	Yes	17.32 ±0.26	0.30
	No	17.89 ±0.5	
Discussed a prospective plan on how to manage your asthma with a physician	Yes	18.08 ±0.29	0.02*
	No	17.01 ±0.33	
Discussed ways on how to prevent asthma symptoms with a physician	Yes	17.84 ±0.32	0.17
	No	17.2 ±0.31	
Discussed ways on how to treat mild and severe symptoms with a physician	Yes	17.51 ±0.36	0.98
	No	17.49 ±0.29	
Has a written treatment plan for asthma attacks	Yes	17.65 ±0.83	0.48
	No	16.98 ±0.28	

† Independent-samples T tests. * indicates significant differences between groups at two-tailed P<0.05.

Table 6. Parsimonious logistic regression model showing odds ratios and 95% confidence intervals for risk variables significantly associated with poorly controlled asthma symptoms (ACT score ≤ 15).

Predictors	Risk level	Estimate	P-value*	OR	95% CI	
					upper	lower
Do you increase or initiate steroid therapy when an attack is perceived? <i>Yes vs. No</i>	Yes	1.57	0.001	4.78	1.88	12.16
Presence of environmental triggers? <i>Bedroom carpets.</i>	Yes	-1.77	0.001	0.17	0.06	0.46
How long you have had asthma? <i><5 years vs. >5 years</i>	<5 years	1.70	0.001	5.47	1.98	15.11
Severity of bronchial asthma classification? <i>Intermittent; Mild persistent; Moderate persistent.</i>	Moderate persistent	1.20	0.001	3.34	1.55	7.19
How do you use the bronchodilator?	[†] Several ways	0.41	0.05	1.51	1.00	2.29
Has your physician discussed a prospective plan on how to manage your asthma? <i>Yes vs. No</i>	No	1.07	0.03	2.91	1.19	4.11
Intercept		0.61	0.72	1.84		

*Wald Chi-square statistic was considered significant at 0.05 level. [†]Possible answer options were: as only therapy for asthma; as rescue therapy, daily; as rescue therapy once per week; as rescue therapy, twice or more/week, and several ways (two or more of the above options). Correlation coefficients for this model: Cox and Snell's $r^2=0.35$; Nagelkerke's $r^2=0.5$; overall percent of cases that are correctly predicted: 81.3%.