

A multicenter survey of childhood asthma in Turkey – II: Utilization of asthma drugs, control levels and their determinants

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Many surveys worldwide have consistently demonstrated a low level of asthma control and under-utilization of preventive asthma drugs. However, these studies have been frequently criticized for using population-based samples, which include many patients with no or irregular follow-ups. Our aim, in this study, was to define the extent of asthma drug utilization, control levels, and their determinants among children with asthma attending to pediatric asthma centers in Turkey. Asthmatic children (age range: 6–18 yr) with at least 1-yr follow-up seen at 12 asthma outpatient clinics during a 1-month period with scheduled or unscheduled visits were included and were surveyed with a questionnaire-guided interview. Files from the previous year were evaluated retrospectively to document control levels and their determinants. From 618 children allocated, most were mild asthmatics (85.6%). Almost 30% and 15% of children reported current use of emergency service and hospitalization, respectively; and 51.4% and 53.1% of children with persistent and intermittent disease, respectively, were on daily preventive therapy, including inhaled corticosteroids. Disease severity [odds ratio: 12.6 (95% confidence intervals: 5.3–29.8)], hospitalization within the last year [3.4 (1.4–8.2)], no use of inhaled steroids [2.9 (1.1–7.3)], and female gender [2.3 (1.1–5.4)] were major predictors of poor asthma control as defined by their physicians. In this national pediatric asthma study, we found a low level of disease control and discrepancies between preventive drug usage and disease severity, which shows that the expectations of guidelines have not been met even in facilitated centers, thus indicating the need to revise the severity-based approach of asthma guidelines. Efforts to implement the control-based approach of new guidelines (Global Initiative for Asthma 2006) would be worthwhile.

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During the last decades, many attempts have been made to improve asthma care, including preparation and distribution of guidelines. Until very recently, asthma guidelines have recommended classification of asthma severity to achieve optimal asthma control using medications to match the individual's level of asthma severity (1). Although asthma control and asthma severity are closely related to each other, they measure distinctly different aspects of the disease.

It is obvious that even good guidelines have no impact on clinical practice unless they are implemented into daily practice or improve the patient's condition. To test the asthma control levels set by the guidelines, a number of surveys, including 'Asthma Insights and Reality' surveys, have been conducted in different populations demonstrating a low level of asthma control and under-utilization of preventive drugs. (2–4) Though these studies have been criticized for being population-based, in which many patients with no or irregular follow-up might have been surveyed, other contributing factors may include the impracticality/complicated structure of the guidelines. As a result of unmet expectations, during 2006, there were intensive efforts to improve asthma guidelines by constructing the treatment approach according to the control status of the patient and developing tools to measure control level more objectively (5, 6).

In 2006, most of the major pediatric asthma centers in Turkey conducted a nationwide study to define the cost and control levels of childhood asthma. Our observations of the control levels and the extent of asthma drug usage form the basis for the present report, which aimed to provide baseline information in a nationwide setting for projecting trends.

Materials and methods

In a multicenter nationwide setting, using a cross-sectional study design, we aimed to investigate the cost and control levels of childhood asthma and their determinants through face-to-face interview based on a structured questionnaire and through a retrospective review of the patients' files.

Study design

In Turkey, most asthmatic children are treated in primary care settings where a regular data recording system for outpatients is unavailable, and thus a retrospective review of patients' files is not possible. Therefore, this study was performed in pediatric asthma outpatient clinics of Turkey, where a file recording system was available for outpatients. Hacettepe University Ihsan Dogramaci Children's Hospital was the study coordinator and invited study centers to participate after announcement of the study protocol, with the aim of including one study center from each city where asthma outpatient clinics exist.

The study protocol was described in detail elsewhere (7). In summary, the study was performed during April 2006 in 12 study centers concurrently and all asthmatic children aged 6–18 yr with scheduled or unscheduled visits during that period were invited to participate in the study.

Though it is not an interventional study, written informed consent approved by the Medical Ethics Committee of Hacettepe University was obtained from all parents and from patients 10 yr of age and older.

Survey instrument

The physicians who performed the interviews were previously given specific training and instruction in the use of the questionnaires, which were validated before. The questionnaire included questions about:

- the demographic characteristics of patients (age, gender, age at the diagnosis of asthma, parental education levels, place of residence)
- the burden of asthma on the patient and the family (In the last year, impact on daily life and success in school, number of missed days from school, missed work days of adult caretakers due to child's asthma, changes at home taken to reduce impact of asthma)
- disease-related characteristics [In the last year, number of planned visits, emergency department (ED) visits, urgent physician visits, hospitalizations—including intensive care, and current asthma medication – inhaled corticosteroids]

teroids (ICS) or oral corticosteroids, long-acting β agonists (LABA), and leukotriene receptor antagonists (LTRA)]

- types of complementary medicine (CM) for asthma.

By reviewing file records, the physicians also noted concomitant allergic and nonallergic diseases, asthma severity, lung function tests, allergies, and their evaluation of asthma control during the last 4 wk.

Data analysis

All data analyses were conducted using SPSS for Windows, version 11.5 (SPSS Inc, Chicago, IL, USA). Results were expressed as the percentage of responses to each question. Simple random sample methods were used to calculate 95% confidence intervals (CIs). Mann–Whitney *U*-test was used to determine relations between asthma control parameters, demographic characteristics, and asthma severity. Bivariate correlation analysis with Spearman correlation coefficients was used for detecting correlations between asthma control parameters and also correlation between physicians' perception of disease control. Variables that were associated with the outcomes in the univariate analysis at a *p* value of less than 0.25 were examined in the multivariate logistic regression models. Backward elimination started with all the variables in the model. Then, at each step, variables were evaluated for entry and removal. The score statistic was always used for determining whether variables should be removed from the model. Wald statistic was used to select variables for removal (by default 0.10). The size of the effect of each of the risk factors was measured by using the odds ratios (ORs) and 95% CIs.

Results

Characteristics

Twelve centers accepted to be involved in the study, and a total of 618 physician-diagnosed asthmatic children with at least a 1-yr follow-up period were included. The majority were males [57.6% (53.1–60.9)], and the mean ($\pm$ s.d.) age was 10.6 ($\pm$ 1.4) yr. Asthma coexisted with allergic rhinitis in 35.9% (32.1–39.7) of patients and 70% (67.3–74.5) of patients were atopic. Additional characteristics of the parents and children are presented elsewhere (7) and summarized in Table 1.

During the 12 months preceding the survey, while patients made 5.3 ± 0.1 scheduled visits, a

Table 1. Patients' demographics (*n* = 618)

Characteristics	
Age, mean $\pm$ s.d.	10.6 $\pm$ 1.4
Gender, male (%)	356 (57.6)
Mean age $\pm$ s.d. at diagnosis of asthma (yr)	5.6 $\pm$ 3.0
Mean duration $\pm$ s.d. of regular follow-up (yr)	3.9 $\pm$ 2.6
Asthma severity <i>n</i> (%)	
Mild intermittent	328 (53.8)
Mild persistent	194 (31.8)
Moderate persistent	78 (12.8)
Severe persistent	10 (1.6)
Allergic rhinitis <i>n</i> (%)	222 (35.9)
Atopic dermatitis <i>n</i> (%)	40 (6.5)
Family history <i>n</i> (%)	
Asthma (one or both parents or sibling)	141 (22.8)
Current smoker in house	203 (32.8)
Father's education (no education/primary school/high school/university)	1.5/22.8/30.3/45.5
Mother's education (no education/primary school/high school/university)	3.9/46.6/28.8/20.7
Atopy <i>n</i> (%)	438 (70.9)
Current drug usage <i>n</i> (%)	312 (50.5)

significant proportion [44.2% (40.1–47.9)] of the children required at least one unscheduled visit, 185 [29.9% (26.3–33.5)] required emergency admittance, and 84 [13.6% (10.9–16.3)] were hospitalized due to asthma.

Asthma control: patients' perspectives

When impact of asthma on daily life and school performance were evaluated, 418 [68.6% (64.9–72.3)] and 216 [35.6% (31.8–39.45)] of parents reported a significant interference, respectively. Three-fourths of the patients (74.6%) could not go to the school at least 1 day because of asthma and a significant proportion of parents (51.3%) also missed work days (Table 2). Multivariate logistic regression model for major impact on daily life due to asthma revealed moderate to severe asthma (OR = 5.9, *p* < 0.001, 95% CI: 2.0–13.8), current hospitalization (OR = 3.32, *p* < 0.05, 95% CI: 1.3–8.2), unscheduled visits (OR = 2.13, *p* < 0.05, 95% CI: 1.3–3.2), and lost school days (OR = 2.01, *p* < 0.05, 95% CI: 1.3–3.0) as major risk factors.

Asthma control: physicians' perspectives

Physicians categorized asthma severity as follows: mild intermittent 53.8% (49.8–57.7), mild persistent 31.8% (28.1–35.5), moderate persistent 12.8% (10.1–15.4), and severe persistent 1.6% (0.63–2.65). Physicians reported that good or complete control of asthma was attained in 86.1% (83.4–88.9) of their patients. Multivariate

Table 2. Asthma control aims and study group findings

Goals	Survey findings
No missed school because of asthma	At least 1 school day missed: 461 (74.6%) Mean number of days missed: 7.6 ± 9.5
No or minimal need for ED visits or hospitalizations	At least 1 unscheduled visit: 273 (44.2%) Mean number of unscheduled visits: 2.4 ± 0.2 At least 1 ED visit: 185 (29.9%) Mean number of ED visits: 2.5 ± 2.2 At least 1 hospitalization: 84 (13.6%)
No impact on daily life	Impact on daily life (%) No: 31.4 Yes, mild/moderate/severe: 38.3/24.6/5.7 Impact on school performance (%) No: 64.4 Yes, mild/moderate/severe: 21.9/11.2/2.5 Father's work at least 1 day lost due to child's asthma: 38.5% Mother's work at least 1 day lost due to child's asthma: 12.8%

logistic regression model for physician-indicated poor asthma control showed that poorly controlled asthmatics were mainly female, had more severe asthma, had usually been hospitalized in the last year, and were not using inhaled steroids either alone or in combination with other preventive medications (Table 3). Physicians' perception of asthma control in the last 4 wk weakly but significantly correlated with impact on daily life as perceived by parents (r_s : 0.331, $p < 0.001$), impact on school performance (r_s : 0.282, $p < 0.001$), missed school days (r_s : 0.284, $p < 0.001$), asthma severity (r_s : 0.372, $p < 0.001$), forced expiratory volume in 1 s (FEV1) (r_s : 0.215, $p < 0.001$), and number of ED admittances (r_s : 0.325, $p < 0.001$) (Fig. 1a).

Asthma severity appeared to be one of the best determinants of asthma control, because a mod-

erate-to-severe asthmatic patient was shown to increase the risk of poor asthma control by 12.6 (5.3–29.8, $p < 0.001$). When compared with mild asthmatics, moderate-to-severe asthmatic children had more scheduled (7.1 ± 0.9 vs. 5.2 ± 0.2) and unscheduled (2.7 ± 0.4 vs. 1.2 ± 0.2) visits ($p < 0.001$) and more admittances to the ED (2.2 ± 0.3 vs. 0.6 ± 0.05) ($p < 0.001$). Parent-perceived disease burden on daily life (93.6% vs. 65.5%) and school performance (67.1% vs. 31.6%) were also higher in moderate-to-severe asthmatics ($p < 0.001$).

Management of asthma

In the whole population, 312 [50.5% (46.5–54.4)] children were on preventive drugs: 147 [23.8% (20.4–27.2)] were on ICS, 37 [6% (4.1–7.8)] on LTRA, 24 [3.9% (2.36–5.4)] on combination of ICS and LTRA, 86 [13.9% (11.2–16.7)] on combination of ICS and LABA, and 18 [2.9% (1.6–4.2)] on combination of ICS, LABA, and LTRA. FEV1% of patients using preventive medication (94.4 ± 1.1) was lower than that of patients not on regular preventive treatment (99.1 ± 1.1) ($p = 0.002$). Treatments were not consistent for any disease-severity group and in each severity group a variety of treatments were documented (Fig. 1b). Almost half of the children in each severity group including mild intermittent asthmatics were on preventive treatments. No preventive treatment was given to 91 (46.9%) mild persistent patients and to 46 (56.3%) moderate-to-severe asthmatic patients. One hundred and forty-one patients (43%) with mild intermittent asthma were using ICS: 49 of those were on combination of ICS and LABA, and five were even on ICS in combination with concurrent LABA and LTRA. In contrast, 30.6% of moderate-to-severe asthmatics were on a single medication like LTRA (4.5%) or ICS (26.1%). There was no difference in medication usage or types of medications due to severity ($p = 0.782$ and 0.809 , respectively). Preventive drug types were not different in relation to physician perception of disease control in the last 4 wk ($p = 0.851$) (Fig. 2). No differences were determined in asthma control parameters, concomitant allergic diseases, age, education levels of parents, asthma in the family, and indoor smoking between preventive drug users and nonusers. Logistic regression analysis for ICS use (either alone or in combination) revealed moderate to severe asthma (OR = 2.0, 95% CI: 1.1–3.4, $p < 0.05$) and physician perception of poor asthma control (OR = 2.9, 95% CI: 1.2–7.2, $p < 0.05$) as predictive factors.

Table 3. Factors leading to poor asthma control in the last 4 weeks

	Multivariate logistic regression model: poor asthma control in the last 4 weeks indicated by physician		
	OR	95% CI	p
Disease severity			
Mild	1 (Ref)		
Moderate to severe	12.6	5.3–29.8	<0.001
Current hospitalization			
No	1 (Ref)		
Yes	3.4	1.4–8.2	<0.05
Use of inhaled steroid			
Yes	1 (Ref)		
No	2.9	1.1–7.3	<0.05
Gender			
Male	1 (Ref)		
Female	2.3	1.1–5.4	<0.05

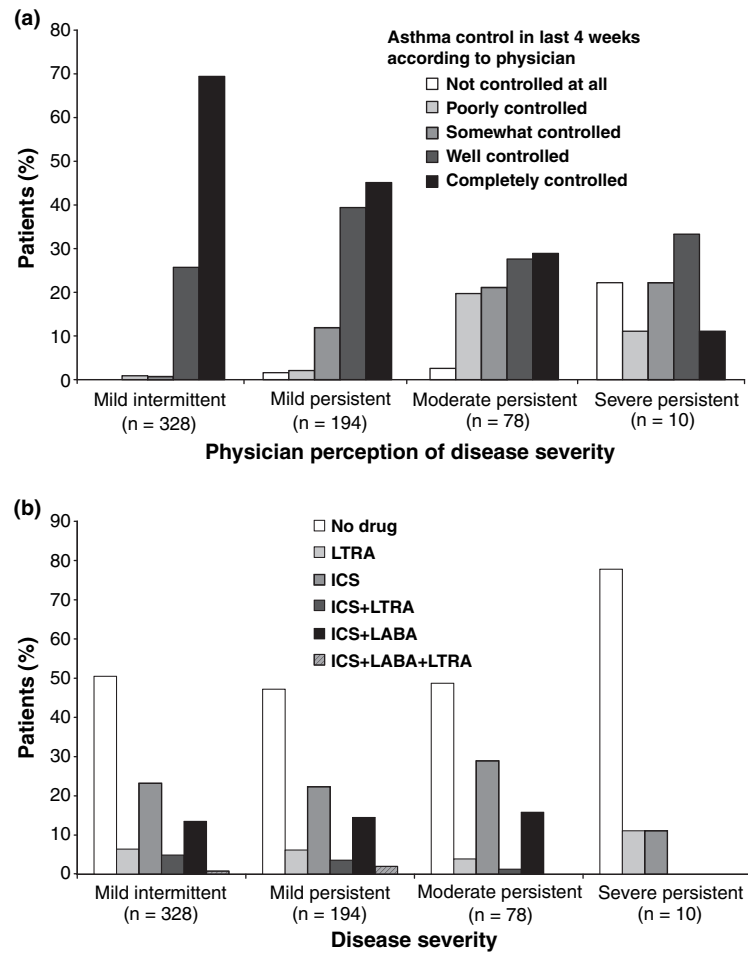


Fig. 1. Physician-perceived control levels of asthma (a) and preventive asthma drug use (b) according to asthma severity.

Complementary medicine (CM)

The prevalence of current use of complementary remedies for asthma was high [45.1% (41.2–49)]. The most commonly reported complementary therapies were honey [32.8% (26.5–37.5)], grape molasses [29.4% (24.5–33.5)], herbal tea [13.8% (9.7–16.3)], and quail eggs [11.6% (7.9–14)].

Determinants of CM use were hospitalization due to asthma in the last year (OR = 1.9, 95% CI: 1.1–3.3, $p < 0.05$) and reported high burden of asthma on daily life as perceived by parents (OR = 1.4, 95% CI: 1.03–2.1, $p < 0.05$). Those who used preventive measures like dust-mite-proof bed covers had a greater tendency to use CM (OR = 1.6, 95% CI: 1.1–2.2, $p < 0.05$).

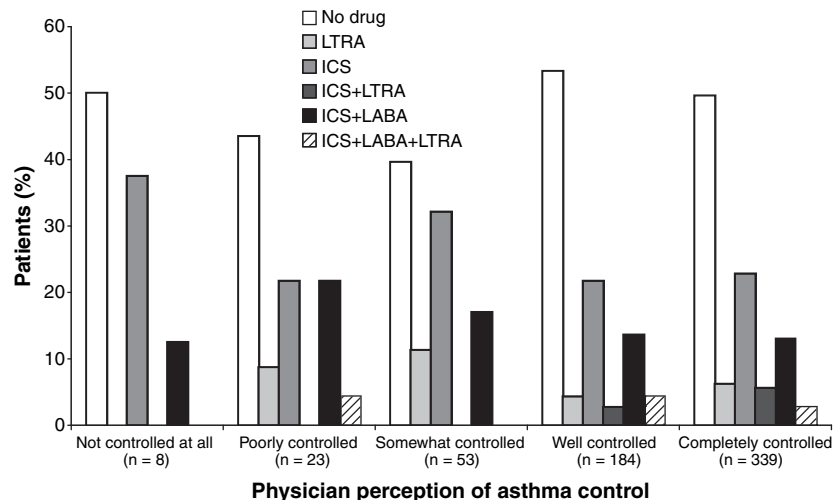


Fig. 2. Preventive asthma drug use according to physician-estimated control level.

Parents' educational status, concomitant allergic disease, anti-inflammatory drug usage, and most importantly asthma severity had no effect on CM use.

Discussion

While several national and international guidelines on management of childhood asthma have been published, little is known regarding the achievement of desired treatment goals, particularly in most facilitated centers. In contrast with previous studies, the survey focused only on asthmatics under regular follow-up and therefore on patients expected to be in a position to obtain optimal treatment and control. Unfortunately, the guideline aims were not met in a substantial number of patients and there was a significant discrepancy between physician-assessed asthma severity and preventive medication use and control levels. Though over-treatment and under-treatment coexist, the latter appeared to be predominant.

Previously, the Asthma Insights and Reality in Turkey (AIRET) survey demonstrated a low level of asthma control in a population-based sample (8). As somewhat expected, the results of the current study showed less burden of asthma on the study group compared to the AIRET study in terms of ED admittance (29.9% vs. 56.4%) and hospitalization (13.6% vs. 26.6%). Interestingly, in the present study, there was higher percentage (74.6 vs. 43.1) of school absenteeism, which logically would be an unexpected finding in a presumably better controlled group. However, we believe that this discrepancy may be explained by the better socio-cultural level of the latter group. Higher expectations and better perception of disease control may explain the observed discrepancy between the two study groups.

In agreement with previous studies (9), our results suggest that the burden of the disease increased when the control was poor. More than 80% of patients with one unscheduled or ED visit reported that asthma had a negative impact on their daily life. Persistent asthma, current hospitalization, school absenteeism, and interference with school performance all contributed to increase in the burden of asthma on daily life. As recommended by currently revised guidelines, if control is used to manage asthma, the expectations and needs of patients will be met easily, which may lead to a decrease in burden on daily life (5).

Female gender appeared to be one of the risk factors for physician-perceived poor asthma

control in the last 4 wk. The observations that women were more likely to have their asthma symptoms inadequately controlled and lower health-related quality of life were also noted in some studies in adults and adolescents (9–12). Poorer prognosis in women has been suggested to relate to differences in lung growth and changes in relative airway diameter and parenchymal size between the sexes. Gender-related perception differences might also have a role (11).

Asthma management guidelines suggest that asthma therapy should improve clinical status, reduce the risk of exacerbations and permanent changes to the airway, enable patients to feel better, and improve daily function (1, 13). In this study, we found that many children with asthma did not receive guidelines-recommended maintenance medication. Only half of the children with persistent asthma were receiving treatment, even those with moderate to severe asthma. Furthermore, one-third of moderate-to-severe asthmatics were using single medication instead of combination therapy. Interestingly, there was no difference in medication usage and types of medication according to asthma severity. Intermittent asthmatics were over-treated; conversely, persistent asthmatics were under-treated. Physician-classified asthma severity was not compatible with physician-planned asthma management, which might be due to incorrect classification, but as asthma severity increased, there was decrease in disease control. This could be explained by low utilization of preventive drugs even in these reference centers. In the AIRE study, there was no correlation between the use of ICS and disease severity (2). Halterman et al. defined moderate to severe asthma as more than two acute visits for wheezing, or more than three episodes of wheezing over the past year, and reported that only 26% of moderate-to-severe asthmatic children in the United States had taken a maintenance medication (14).

In many chronic diseases, management goals guide the treatments irrespective of disease severity. The National Heart Lung and Blood Institute (NHLBI) recommended severity as a tool to direct management, but severity classification was not practical and complicated (1). In another study on knowledge and attitude of Turkish physicians treating asthmatic children, it was shown that assessment of asthma severity was the least understood part of the guidelines (15). Most asthmatics are followed by primary care physicians who are in need of simple and practical guidelines that are easy to follow. Now, Global Initiative for Asthma (GINA) 2006 recommends classification of asthma by severity

only for research purposes. Instead, it focuses on a classification of asthma by level of control: controlled, partly controlled, or uncontrolled (5). In this study, more than 80% of physicians concluded that their patients were under control, but the level of control was inconsistent with the low objective parameters of asthma control. Interestingly, preventive medication types did not differ between physician perception of controlled or uncontrolled patients in the last 4 wk. There is need for an objective, reliable tool to improve the communication between physicians and patients and to assess and monitor accurate control levels.

Complementary treatments were used in more than 40% of cases during the last year, particularly in children whose asthma had a negative impact on their daily life and caused hospitalization within the last year. This is in agreement with Orhan et al., who reported that poor asthma control appeared to be the leading predictor of CM use (16). Particularly in children, fear of adverse effects of corticosteroids, dissatisfaction with conventional medicine, and low success rate experienced in asthma treatment might be responsible for the high prevalence of CM usage. We determined that disease severity had no effect on CM usage or preference. Andrews et al. was also unable to detect any relationship between CM use and asthma severity (17), but some other researchers found severity to be an important determinant of CM use (18, 19).

There are some limitations to our study. First, we relied on parental or patient recall, and thus a reporting bias cannot be completely excluded. In addition, data on medications were only based on declarations, which might not reflect the actual use of the drugs by the patients. Their adherence to antiasthma medication could not be assessed.

In conclusion, in this national, multicenter study, we have highlighted an inadequate level of asthma control in children and discrepancies between the preventive drug usage and disease severity when asthma control goals were considered. There is need for collective collaboration of physicians, parents, and children. Physicians dealing with asthma management should spend more time to understand their patients' asthma control level to make treatment plans as recommended by GINA 2006 in order to meet patient expectations. Educational programs and public health resources should be targeted to better application of asthma management guidelines with regard to both under-treatment and aggressive treatment, and to parental education to increase awareness of the significance of recognizing persistent asthma symptoms to decrease

attack rate, hospitalizations, and readmissions (20) and using preventive medications to decrease significant morbidity among children with asthma.

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Sekerel BE had primary responsibility for protocol development and outcome assessment, contributed to data analysis, and prepared the manuscript with *Soyer OU*.

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