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# Potential predictors of relapse after treatment of asthma exacerbations in children

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#### ABSTRACT

**Background:** Knowledge of factors that affect relapse will allow close monitoring of patients at risk, resulting in a decreased rate of readmission to the emergency department.

**Objective:** To determine risk factors associated with relapse within 7 days after treatment of asthma exacerbations in children.

**Methods:** This was a multicenter, prospective study of children with asthma attacks. Patients between the ages of 6 months and 17 years who met the criteria between June 2009 and September 2012 were considered.

**Results:** The study included 1177 patients (775 males [65.8%]) with a mean (SD) age of 70.72 (48.24) months. Of them, 199 (16.9%) had a relapse within 1 week after being discharged from the hospital. Factors independently associated with relapse identified by a logistic regression model for the 1,177 study visits were having taken a short-acting inhaled  $\beta_2$ -agonist within 6 hours before admission (odds ratio [OR], 2.43; 95% confidence interval [CI], 1.728-3.426; P = .001), presence of retraction on physical examination (OR, 1.76; 95% CI, 1.123-2.774; P = .01), no prescription for high-dose inhaled steroids on release (OR, 2.02; 95% CI, 1.370-3.002; P < .001), and not being given a written instructional plan (OR, 1.55; 95% CI, 1.080-2.226; P = .02). **Conclusion:** Whereas having taken short-acting  $\beta_2$ -agonists within 6 hours before admission and the presence of retractions on physical examination increased the risk of relapse after treatment of the acute attack, being given high-dose inhaled steroids and a written instructional plan when being sent home reduced the risk.

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# Introduction

Asthma is the most common chronic disease in childhood; its prevalence is estimated to be 5% to 10%. 1-3 Asthma attacks account for 6% of the cases admitted to the pediatric emergency department. 4-6 A few studies have tried to determine the revisit rate and risk factors associated with this in the short-term follow-up of patients after asthma attacks. Risk factors identified have included age younger than 2 years, persistent asthma, frequent admission to the hospital with asthma attacks in the previous year, and lower asthma quality-of-life scores. 7-10 Knowledge of the factors that affect relapse will allow close monitoring of patients at risk, resulting in a decreased rate of readmission to the emergency department. Decreased emergency department readmissions will provide better quality of life, less absenteeism from school for children,

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less absenteeism from work for parents, and a decrease in the costs of treatment.

The objective of our study was to identify variables associated with the relapse of asthma symptoms within 7 days after an initial treatment for an asthma exacerbation. We sought to identify unique factors and also to assess whether factors identified in previous studies were significant.

# Methods

Study Design

Patients diagnosed as having asthma attacks who were admitted to the pediatric emergency departments and the pediatric allergy and asthma departments at 3 teaching and research hospitals (Gazi University Faculty of Medicine, Gülhane Military Medical Academy, and the Medical School, Diskapi Education and Research Hospital) from June 2009 to September 2012 and who met the study criteria were entered into the study.

The patients who were included were between the ages of 6 months and 17 years, had been diagnosed previously as having

asthma by a physician, or had a history of at least 3 wheezing attacks that necessitated treatment with short-acting  $\beta_2$ -agonists, and patients with mild or moderate asthma attacks at admission.

Patients younger than 6 months or younger than 2 years in the season of the respiratory syncytial virus infection, severe attack at admission, chronic lung disease (cystic fibrosis or bronchopulmonary dysplasia), or cardiac disease (congenital heart disease) comorbid with diagnosed asthma and/or wheezing attacks; those with a history of premature birth; those with a birth weight of less than 2,500 g; those who underwent asthma attack treatment at the emergency department within 7 days before admission; patients in whom treatment with  $\beta_2$ -agonists and/or corticosteroids was contraindicated; and those who had severe or life-threatening asthma attacks were excluded from the study. In addition, patients whose symptoms continued because they did not take the given treatment were excluded.

Patients enrolled into the study and their parents were questioned. Patient demographic features, patient histories, asthma histories, the nature of previous asthma attacks, the controller medication they were using, the attack medications they used immediately before presenting to the emergency department, physical examination signs, and treatment administered at the emergency department and when being sent home were recorded in a previously prepared survey form. The severity of the attack and the decision on hospitalization of patients who were admitted to the hospital with an asthma attack were determined according to the Global Initiative for Asthma (GINA)<sup>11</sup> guidelines. Patients who were treated and sent home were advised to return in cases of increased, or not reduced, symptoms despite taking the treatments.

The families of patients were contacted by the researchers (E.T., O.A.G., and M.A.) 7 days after the patients were discharged from the hospital. Information regarding the continuity of symptoms, such as cough, wheezing, and shortness of breath, drug use, and revisits to a physician, were ascertained from these interviews and the survey completed.

# Definitions

Asthma attack is defined as an episode of progressive increase in shortness of breath, cough, wheezing, or chest tightness or some combination of these symptoms. Severe asthma attack is defined as a potentially life-threatening attack that requires close supervision. Relapse is worsening of symptoms (eg, cough, wheezing, shortness of breath, and chest tightness) or revisiting a physician because of no decrease in the symptoms despite treatment after the patient was treated for the asthma attack and discharged from hospital. The severity of the asthma attack in the patients who presented with an asthma attack was categorized as mild, moderate, severe, or life-threatening, according to GINA. Choice of treatment according to the severity of the attack was also determined according to GINA.

Patients newly diagnosed or those already diagnosed as having asthma and who did not use a controller medication regularly, taking into consideration their complaints in the last 3 months, had the *severity of asthma* categorized as intermittent, mild-persistent, moderate-persistent, and severe-persistent, according to GINA. Asthma control was categorized in patients taking a controller medication regularly, taking into consideration their symptoms in the last 3 months, as asthma controlled, partially controlled, or uncontrolled, according to GINA. Controller medication refers to the long-term use of inhaled corticosteroids, leukotriene receptor antagonists, long-acting  $\beta_2$ -agonists, and the use of one or more of these medications to control asthma-related symptoms. High-dose inhaled steroid treatment is the use of more than 1,000  $\mu$ g/d of nebulized budesonide. Short-acting  $\beta_2$ -agonists and high-dose inhaled steroids were prescribed in mild asthma attacks.

Short-acting  $\beta_2$ -agonist, high-dose inhaled steroids, and systemic steroids were prescribed in moderate asthma attacks.<sup>11</sup>

## Predictor Variables

Potential risk factors that could be associated with relapse were evaluated statistically. These included demographic data (age, sex, exposure to cigarettes, and having used breast milk for <6 months), history of asthma (being under regular follow-up by an allergy specialist, severity of asthma, level of control, preventive treatment taken, time of the last attack, number of attacks in the previous year, number of attacks requiring systemic steroids, and number of attacks requiring hospitalization), information about the attack (being given short-acting  $\beta_2$ -agonists within 6 hours before admission and severity of the attack at admission), signs on physical examination (retractions and oxygen saturation), treatment given at the hospital, drugs prescribed when discharged from the hospital, and whether an instructional plan was provided.

The research protocol was approved by the Ethics Committee of Gazi University Faculty of Medicine (No. 5295; date, 6.15.2009). All participants (parents and children >12 years old) provided written informed consent.

## Statistical Analysis

Statistical analyses were performed using the SPSS software (version 15; SPSS Inc, Chicago, Illinois). Categorical variables were compared using a  $\chi^2$  test, and quantitative variables were compared using the Mann-Whitney test. A 2-sided P<.05 was considered to indicate statistical significance. A logistic regression model was constructed. In the model, multivariate analysis was used, including statistically significant variables from the univariate analyses and/or important parameters (eg, no prescription of highdose inhaled steroids and no provision of a written care plan) to identify factors that affect relapse after being treated.

### Results

During the study period, 1,476 patients with an asthma attack were admitted to the pediatric emergency departments or pediatric allergy asthma departments. In total, 1,177 patients who met the study criteria and who could be contacted for follow-up were included (Fig 1). Of the patients, 775 (65.8%) were male, with a mean (SD) age of 70.72 (48.24) months. Of the patients, 827 (70%)

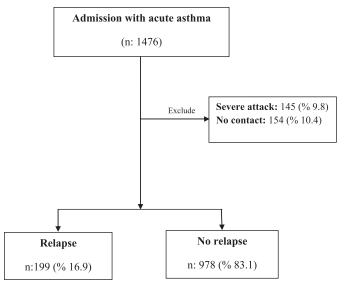


Figure 1. Flow diagram of children with acute asthma included in the study.

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