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Prognosis of adult asthma: a 7-year follow-up study

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ABSTRACT

Background: Studies on adult-onset asthma and the contributing factors for its prognosis are few in the literature.**Objective:** To evaluate asthma prognosis, remission rate, and contributing factors in an adult patient population.**Methods:** Two hundred patients with a diagnosis of adult-onset asthma in 2006 were included in this study. Of these, 160 were contacted in 2013 and participated in the study. Their demographic features, family history, clinical symptoms, pulmonary function test results, and Asthma Control Test scores were re-evaluated. Patients' asthma control status was determined. Patients who had total control and had not used any asthma treatment for at least 2 years were classified as in remission.**Results:** The study group consisted of 160 patients (144 women and 16 men, mean age 52.9 ± 10.3 years). Nearly 70% of patients had adult-onset asthma before 40 years of age. According to asthma control status, 21.9% of patients had uncontrolled asthma, 29.4% had partially controlled asthma, and 48.8% had totally controlled asthma. Remission was observed in 11.3% of the entire study group. The mean age of the remission group was significantly younger. Disease duration was shorter and the proportion of patients with atopy was larger in the totally controlled and remission groups. Except in the remission group, patients showed weight gain from 2006 through 2013.**Conclusion:** According to these 7-year follow up data, the remission rate of asthma was 11.3%. Patients with younger age, younger onset, atopy, allergic rhinitis, and few comorbidities seemed to have a greater possibility of remission.

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Introduction

An estimated 300 million people worldwide have asthma. Despite advances in asthma treatment, it is not a curable disease. With suitable treatment, patient compliance, and regular visits, clinical control of symptoms is possible for most patients. In contrast to childhood asthma, little is known about the course of asthma activity in adults and the prognosis of adult-onset asthma is unknown; very few publications exist concerning remission rates. The goal of treatment in asthma is control of disease. One end of the treatment spectrum is achieving the goal of a remission state, but there are different definitions of what is meant by remission. Most publications have defined remission as an absence of asthma symptoms without current pharmacologic therapy.¹ In a recent prospective epidemiologic study, remission was defined as no asthma symptoms in 2 consecutive years and no current asthma treatment. The distinction between clinical and complete remission is has been defined further by the

presence or absence of bronchial hyperresponsiveness and airway obstruction. Patients who lack bronchial hyperresponsiveness and airway obstruction in combination with a lack of symptoms and no pharmacologic therapy are defined as being in complete remission. However, a substantial proportion of patients in clinical remission who continue to have bronchial hyperresponsiveness might have rebound symptoms later in life,² although a small percentage of young adults in clinical remission remain asymptomatic for the rest of their lives.² These patients and those in complete remission can be defined as having true remission.³

The authors evaluated remission rates and prognosis in a population of adult patients with asthma and assessed factors that influenced their prognosis.

Methods

The clinical records of patients who were diagnosed in 2006 as having asthma in accordance with the Global Initiative for Asthma (GINA) guidelines⁴ were screened and 980 files were identified. The authors searched for patients in this group who had been admitted to the outpatient clinic in 2013 with asthma and had 7 years of follow-up. Two hundred patients were identified who fulfilled these criteria.

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Patients' demographic features, smoking habits, atopy status, body mass index (BMI), comorbidities, family history, pulmonary function test results, and asthma medications were reviewed.

An attempt was made to contact the 200 patients and they were invited for re-evaluation. Forty patients could not be reached because their telephone numbers had changed or the call was not answered after 3 attempts. One hundred sixty patients accepted the request to participate in this study and they were re-evaluated from October through December 2013. All analyses were performed in these 160 patients.

To assess their disease control status with respect to the GINA 2012 guidelines, all patients were interviewed regarding day and night symptoms, rescue medication use, and limitation of activity during the previous 1-month period. They also were asked about exacerbation, hospitalization, and frequency of use of emergency medical treatment during the previous year and the previous 7 years. The Asthma Control Test (ACT) was completed by all subjects. Subjects with an ACT score of 25 were considered as having total control, those with a score from 20 to 24 were considered as having partial control, and those with a score lower than 20 were classified as having uncontrolled asthma.⁵ The authors assessed the concordance of control status of the ACT score and the GINA criteria in all patients. For the few patients whose control status was inconsistent with the ACT score and the GINA criteria, their results were assigned to the lower control parameter. Patients who were considered as have totally controlled asthma also were evaluated for remission status; patients who had no asthma symptoms and had used no asthma treatment for at least 2 years were classified as being in clinical remission. They were asked to undergo bronchial provocation tests (BPTs) using methacholine with a KoKo Dosimeter (nSpire Health, Inc, Longmont, Colorado) to assess whether their asthma was in complete remission.

Pulmonary function tests were performed using a ZAN 100 spirometry device (nSpire Health, Inc). Pulmonary function tests (forced expiratory volume in 1 second [FEV₁], forced vital capacity, peak expiratory flow, and maximum mid expiratory flow [MMF]) were measured and evaluated in accordance with guidelines of the American Thoracic Society and the European Respiratory Society.

The patients' weight and height were measured and their BMIs were calculated. Patients with a BMI of at least 30 kg/m² were

considered obese. Obesity was classified as class 1 (BMI 30–34.9 kg/m²), class 2 (BMI 35–39.9 kg/m²), or class 3 (BMI > 40 kg/m²). Patients' BMI, FEV₁ (milliliters [FEV₁-mL] and percentage predicted [FEV₁-%p]), and MMF (milliliters [MMF-mL] and percentage predicted [MMF-%p]) of 2006 were compared with those of 2013.

This study was conducted in accordance with the amended Declaration of Helsinki. Written informed consent was obtained from all participants. The study was approved by the medical ethics committee of the Ankara University School of Medicine (Ankara, Turkey; approval number 18-687-13).

Statistical Analysis

Statistical analyses were performed using SPSS 20.0 (SPSS, Inc, Chicago, Illinois). Numeric values with normal dispersion were expressed as mean $\pm$ SD, whereas variables with abnormal dispersion were expressed as median (minimum and maximum). Categorical variables values were expressed as number (percentage). The Student *t* test was used to compare the 2 groups by age. The importance of the difference according to mean values between groups was examined with analysis of variance. The χ^2 tests were used for the comparison of 2 independent groups for categorical data. All directional *P* values were 2-tailed and significance was assigned to values lower than .05.

Results

Initially, 200 patients with a 7-year follow-up history were identified for review of demographic features. Their mean age was 52.2 $\pm$ 11.1 years and the female-to-male ratio was 87.5% (*n* = 175) to 12.5% (*n* = 25). Asthma onset occurred before 40 years of age in 70% (*n* = 140) of patients. The ratios of smokers, ex-smokers, and nonsmokers were 8% (*n* = 16), 12.5% (*n* = 25), and 79.5% (*n* = 159). Family history was positive in 42% (*n* = 84) of patients and 49.5% (*n* = 99) had positive skin prick test reactions for at least 1 inhalant allergen. Half the study group (50.5%, *n* = 101) had comorbid diseases, such as diabetes mellitus, hypertension, cardiovascular diseases, thyroid disorders, psychiatric diseases, rhinitis, sinusitis, nasal polyposis, and urticaria. Thirty-eight percent (*n* = 76) of patients were obese.

Table 1
Demographic characteristics of 160 patients who were contacted in 2013 vs total population and 40 patients who could not be reached

	Total population (N = 200)	Patients reached in 2013 (n = 160)	Patients not reached in 2013 (n = 40)
Age (yr), mean $\pm$ SD	52.2 $\pm$ 11.1	52.9 $\pm$ 10.3	49.4 $\pm$ 16.6
Age at onset (y), mean $\pm$ SD	35 $\pm$ 11.4	35.8 $\pm$ 11.4	32.4 $\pm$ 11.8
Sex, n (%)			
Men	25 (12.5)	16 (10)	9 (22.5)
Women	175 (87.5)	144 (90)	31 (77.5)
Asthma onset at <40 y, n (%)	140 (70)	109 (68.1)	31 (77.5)
Family history, n (%)	84 (42)	67 (41.9)	17 (42.5)
Comorbidities, n (%)	101 (50.5)	86 (53.8)	15 (37.5)
Atopy, n (%)	99 (49.5)	78 (48.8)	21 (52.5)
Allergy to pollens	51 (51.5)	42 (53.8)	9 (42.8)
Allergy to <i>Dermatophagoides</i> spp	68 (68.6)	54 (69.2)	14 (66.6)
Allergy to other allergens	31 (31.3)	28 (35.8)	3 (14.2)
Rhinitis, n (%)	95 (47.5)	75 (46.9)	20 (50)
Obesity groups, n (%)			
Normal weight	47 (23.5)	37 (23.1)	10 (25)
Overweight	70 (35)	54 (33.8)	16 (40)
Class 1 (BMI 30–34.9 kg/m ²)	50 (25)	44 (27.5)	6 (15)
Class 2 (BMI 35–39.9 kg/m ²)	21 (10.5)	20 (12.5)	1 (2.5)
Class 3 (BMI $\geq$ 40 kg/m ²)	5 (2.5)	5 (3.1)	0
Smoking habit, n (%)			
Nonsmokers	159 (79.5)	129 (80.6)	30 (75)
Active smokers	16 (8)	11 (6.9)	5 (12.5)
Ex-smokers	25 (12.5)	20 (12.5)	5 (12.5)

Abbreviation: BMI, body mass index.

Research staff was able to contact 80% (160 of 200) of the identified patients, all of whom agreed to participate in the study. Forty patients could not be contacted. Table 1 presents the demographic and clinical characteristics of the re-examined and uncontacted groups.

According to asthma control status, 21.9% ($n = 35$) of patients had no control, 29.4% ($n = 47$) had partial control, and 48.7% ($n = 78$) had total control.

When patients in the total control group were evaluated for remission, 23.1% ($n = 18$) were determined to be in a remission state. This was 11.3% of the entire study population ($n = 18$ of 160). Nine patients with remission who agreed to undergo BPT were examined for the presence of bronchial hyperreactivity. Three of these 9 patients achieved normalization of bronchial hyperreactivity against methacholine and were classified as being in complete remission. The other 6 patients still had bronchial hyperreactivity and were considered in clinical remission.

The 3 control asthma status groups (uncontrolled, partially controlled, and totally controlled) were compared with the remission group. There was no relation between asthma control status and sex, age of asthma onset, family history, smoking habit, and BMI. The asthma of most patients in remission began before they were 40 years old (72.2%, $n = 13$). The mean age at asthma onset in this group was 33 ± 11.5 years. This was not significantly different from the other control status groups (uncontrolled, 34.5 ± 12 years; partially controlled, 36 ± 10 years; totally controlled, 37 ± 11 years; $P = .6$). The mean age of the remission group (45.8 ± 12 years) was significantly younger than the uncontrolled (55.9 ± 10.5 years), partially controlled (53 ± 9.6 years), and totally controlled (53 ± 9.7 years) groups ($P < .05$). Disease duration was shorter in the remission and totally controlled groups than in the uncontrolled group ($P = .01$ and $P = .05$, respectively). In the totally controlled and remission groups, the proportion of patients with atopy was larger than in the partially controlled and uncontrolled groups but this was not statistically significant (66.7%, 55% vs 44.7%, 34.3%). There was no difference in the distribution of allergen sensitivity between groups. The frequency of rhinitis was 46.9% ($n = 75$ of 160) in the totally controlled group. Patients in remission had the fewest comorbid conditions (27.8% of patients) but the difference between groups was not statistically different ($P = .06$).

The mean BMI values were higher in 2013 than in 2006 (30.2 vs 28.7 kg/m²; $P < .05$; Table 2). When the uncontrolled, partially controlled, totally controlled, and remission groups were evaluated according to mean BMI value, there was no significant difference among groups in 2006 or 2013. For weight gain, there was no significant increase in the remission group during the 7 years of follow-up in contrast to the significant weight gain in the totally controlled, partially controlled, and uncontrolled groups from 2006 to 2013. The increases in BMI in the uncontrolled, partially controlled, and totally controlled groups were 2.1, 1, and 0.8 U, respectively ($P < .01$).

Table 2
Comparison of the data of 160 patients between 2006 and 2013

	2006	2013
Mean age	52.9 ± 10.3	45.2 ± 11.1
Mean BMI	28.7 ± 5.3	30 ± 5.6
Mean FEV ₁ , %	78.4 ± 18.9	82.1 ± 21.4
Mean FEV ₁ , mL	1.97 ± 0.6	2.01 ± 0.6
Mean MMF, %	53.3 ± 23.2	53.8 ± 25.8
Mean MMF, mL	1.7 ± 0.8	1.7 ± 0.9
Obesity groups		
Normal weighted, n/%	37/23.1	28/17.5
Overweighted, n/%	54/33.8	48/30
Class-1 (BMI: 30–34.9), n/%	44/27.5	54/33.8
Class-2 (BMI: 35–39.9), n/%	20/12.5	19/11.9
Class-3 (BMI: ≥ 40), n/%	5/3.1	11/6.9

According to the 7-year follow-up spirometric results, the mean FEV₁-mL and FEV₁-%p values of the patients were higher in 2013 than in 2006 (1.97 mL and 78.4% vs 2.01 mL and 82.2%; $P < .05$; Table 2). There was a significant increase in mean FEV₁-mL (0.2 mL, $P = .01$) and FEV₁-%p (9.6 U, $P = .003$) in the remission group. MMF-mL and MMF-%p also were increased (0.17 mL, 4.6 U), but this was not statistically significant ($P = .1$). In the uncontrolled group, there were decreases in FEV₁-mL, FEV₁-%p, MMF-mL, and MMF-%p values (0.22 mL, $P = .002$; 7.8 U, $P = .008$; 0.26 mL, $P = .002$; 6.9 U, $P = .006$, respectively). In the partially and totally controlled groups, FEV₁-%p was significantly increased at 5.9 and 6.9 U, respectively ($P < .005$). FEV₁-mL also was increased in the partially and totally controlled groups but was not statistically significant in the partially controlled group ($P = .1$ and $P = .01$, respectively). FEV₁-mL, FEV₁-%p, MMF-mL, and MMF-%p values were higher in patients in remission than in the others in 2006 and 2013 ($P < .05$).

Discussion

The remission rate in adult patients with asthma was found to be 11.3% in this 7-year follow-up study. There are few studies on remission of asthma in adults and they have different results.⁶ Several disparate definitions of remission have been used, which could explain in part the difference in remission rates among studies. In the present study, remission was defined as no current use of asthma medication and no asthmatic symptoms during the previous 2 years.⁷ Similar to the present data, European Community Respiratory Health Surveys 1 and 2 indicated that the percentage of adults with asthma in remission at the end of 9 years of follow-up was 11.9%.⁷ The present results together with those of previous reports show quite a heterogenous picture, with remission rates of 6% to 21% in adults with asthma.^{8–10}

The goal of asthma management, according to the GINA guidelines, is to achieve symptom control. When patients were evaluated in accordance with the criteria of the GINA guidelines coupled with the ACT score, the proportion of patients with an ACT score of at least 20 was found to be 78% in the present study population, with 48% of them having total control. In a recent study from Turkey, nearly half the study group (51.5%) was reported to have controlled asthma.¹¹ This was in parallel with 2 other reports in which total control rates were 55% and 48%, respectively.^{12,13} The percentage of patients with controlled asthma seems to be larger in the present study than in the cited studies. This might be explained by the fact that the present study population was regularly followed in an asthma clinic of a university hospital.

Like most published studies, patients with remission in the present study were younger than those in the other control status groups. It has been shown that younger patients have a better chance to alleviate their symptoms or might even outgrow asthma.⁷ In the Swedish part of the European Community Respiratory Health Surveys, young age appeared to predict remission.¹⁴ For age of onset, the results were contradictory.^{1,15} In the present study, patients with remission had a younger age at onset but this did not reach statistical significance.

Several studies have reported a negative relation between the presence of allergic rhinitis and being in remission state.^{15,16} In contrast to these findings, the proportions of patients with allergic rhinitis and atopy were quite high in the remission group (61.1% and 55%, respectively). However, the authors found no difference when the groups were compared according to sensitization to different aeroallergens. As expected, comorbidities other than allergic rhinitis were seen the least in the remission group.

With the exception of the remission group, this study found an increase in BMI of most patients during the 7-year follow-up. Although the BMI of the patients with uncontrolled asthma increased more than that in those with remission, the difference was

not statistically significant. This trend also was found in a 9-year European longitudinal study, which reported that patients who achieved remission were those who gained the least amount of weight during the follow-up period.^{10,17} The literature also indicates a significant relation between asthma control and obesity. Asthma course was found to be more severe in obese patients and significant improvement could be achieved after weight loss.¹⁸ The present findings, in parallel with the European study, suggest that patients who do not gain weight have a better chance of attaining a totally controlled status or even a remission state.

Studies of children have shown that better lung function is significantly associated with better prognosis during adulthood.^{19,20} Higher FEV₁ values at the first visit and during remission have been reported to be important predictive factors for children with asthma who develop clinical remission.²¹ Several studies in adults have suggested that longer duration of asthma and severe disease are associated with an FEV₁ decrease and irreversible airway obstruction.^{22,23} In the present study, FEV₁-mL, FEV₁-%p, MMF-mL, and MMF-%p values were highest in the remission group in 2006 and 2013. Moreover, there was an increase in FEV₁ in the controlled groups, which was highest in the remission group during follow-up. According to these results, better lung function at baseline and preserved FEV₁ during follow-up predict a good prognosis. The authors believe that the evaluation of pulmonary function test results over a 7-year follow-up period is a strength of their study. In a large 9-year follow-up study, asthma control was shown to be an important predictor of asthma remission.²⁴ In the present study, the authors found that FEV₁ also is a good predictor of being in remission.

Several limitations of the study should be highlighted. The most remarkable limitation is the lack of BPTs in the entire study population. Only 50% of patients in remission underwent BPT, which limits the value of the data of those who had BPT compared with the entire group. However, normalization of bronchial hyperresponsiveness has not always featured in the disparate definitions of remission that have previously been used. Another limitation of the study is the relatively small size of the study population; participants were included on the condition that they were still under follow-up in 2013, which could have limited the size of the study population because this was a 7-year follow-up study. The effect of the presence of comorbid diseases on prognosis could not be evaluated definitively because the presence of new additional comorbidities was not discussed in 2013 and a comparison between the 2 periods was not performed.

In conclusion, childhood asthma is generally considered to have a high remission rate. However, studies that have evaluated remission in adults with asthma are scarce. The present study demonstrates that adults with asthma, albeit at a low rate, have a chance of being in remission. Patients with a younger age, a younger age at onset, higher FEV₁ levels, lower BMI values, atopy, allergic rhinitis, and few comorbidities seem to have a greater possibility of remission. Further studies are needed to suggest the role of these factors in predicting remission in adult-onset asthma.

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