



# Reflux, Allergic Rhinitis, and Sleep Disorders with Asthma Control and Quality of Life

## Reflü, Alerjik Rinit ve Uyku Bozukluklarının, Astım Kontrolü ve Yaşam Kalitesi İle İlişkisi

Astım ve Komorbiditeler / Asthma and Comorbidities

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### Özet

**Amaç:** Bu çalışmada, Türk astmatik hastalarda gastroözefageal reflü, alerjik rinit ve uyku bozukluklarının, astım kontrolü ve astım yaşam kalitesi ile ilişkisinin araştırılması amaçlanmıştır. **Gereç ve Yöntem:** Çalışmaya astım tanısı ile takip edilen 50 hasta alınmıştır. Başvuru sırasında spirometrik parametreler, Reflü Semptom İndeksi (RSİ), Alerjik Rinokonjonktivit Semptom İndeksi (ARSİ), Pittsburgh Uyku Kalitesi İndeksi (PUKİ), Astım Kontrol Testi (AKT) ve Astım Yaşam Kalitesi Ölçeği (AQLQ) bir doktor gözetiminde dolduruldu, ayrıca sigara alışkanlığı, vücut kitle indeksleri kaydedildi. Spirometrik parametreler ile RSİ, ARSİ ve PUKİ ile AQLQ ve AKT arasındaki ilişki SPSS 15.0 istatistik programı kullanılarak değerlendirildi. **Bulgular:** AKT ve RSİ arasında ( $r = -0.314$ ,  $p = 0.026$ ) ve de AKT ve PUKİ arasında negatif korelasyon ( $r = -0.620$ ;  $p < 0.001$ ) saptandı. AKT ve AQLQ arasında pozitif korelasyon saptanırken ( $r = 0.667$ ,  $p < 0.001$ ), AKT ve ARSİ arasında ilişki saptanmadı ( $p = 0.25$ ). AQLQ ve RSİ arasında ( $r = -0.551$ ;  $p < 0.001$ ) ve de AQLQ ve ARSİ arasında ( $r = -0.390$ ;  $p < 0.005$ ) negatif korelasyon saptandı. AQLQ ve PUKİ arasında ve ayrıca FEV1 değeri ile AKT, AQLQ, RSİ, ARSİ ve PUKİ arasında ilişki saptanmadı. **Tartışma:** Sonuç olarak gastroözefageal reflü ve alerjik rinit astımlı hastalarda yaşam kalitesini ve astım kontrolünü olumsuz yönde etkilemektedir, ayrıca kötü uyku kalitesi kötü astım kontrolü ile ilişkilidir.

### Anahtar Kelimeler

Astım Kontrol Testi; Astım Yaşam Kalitesi; Gastroözefageal Reflü; Alerjik Rinit; Uyku Bozuklukları

### Abstract

**Aim:** In this study we aimed to investigate the effect of comorbid diseases such as gastroesophageal reflux, allergic rhinitis, sleep disorders with asthma control test and asthma quality of life in Turkish asthma patients. **Material and Method:** Total of 50 patients who were followed with a diagnosis of asthma were enrolled in this study. During application, spirometric parameters, Reflux Symptom Index (RSI), Allergic Rhinoconjunctivitis Symptom Index (ARSI), Pittsburgh Sleep Quality Index (PSQI), Asthma Control Test (ACT), and Asthma Quality of Life Questionnaires (AQLQ) were filled under the supervision of a physician, also smoking habits, body mass index of cases were recorded. The relation of spirometric parameters, RSI, ARSI and PSQI with AQLQ and ACT tests were investigated by using SPSS 15.0 statistical software. **Results:** Negative correlation was found between the ACT and RSI ( $r = -0.314$ ,  $p = 0.026$ ), ACT and PSQI ( $r = -0.620$ ;  $p < 0.001$ ). Positive correlation was found between ACT and AQLQ ( $r = 0.667$ ,  $p < 0.001$ ), there was no relationship between ACT and ARSI ( $p = 0.25$ ). Negative correlation was found between AQLQ and RSI ( $r = -0.551$ ;  $p < 0.001$ ), AQLQ and ARSI ( $r = -0.390$ ;  $p < 0.005$ ). There was no relationship between AQLQ and PSQI ( $p = 0.082$ ), also there was no relationship between FEV1 value and ACT, AQLQ, RSI, ARSI, PSQI. **Discussion:** In conclusion, gastroesophageal reflux and allergic rhinoconjunctivitis negatively effect the quality of life and asthma control in asthmatic patients, also poor sleep quality is associated with poor asthma control.

### Keywords

Asthma Control Test; Asthma Quality Of Life; Gastroesophageal Reflux; Allergic Rhinitis; Sleep Disorders

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## Introduction

Comorbid conditions among patients with asthma are common and may decrease the quality of life and are associated with adverse behavioral and psychosocial affects [1]. Also, despite therapeutic progress, the morbidity and mortality of asthma is substantial since some comorbidities influence the management of this chronic disease. Therefore, finding and elimination of these influencing factors are one of the priorities. There is a considerable evidence that, special medical conditions affect asthma managing, such as gastroesophageal reflux, allergic rhinitis, infections, surgery, obesity related comorbidities like obstructive sleep apnea [2-6].

Association of asthma with gastroesophageal reflux and allergic rhinitis is well known. Cheung and his colleagues showed that a significant proportion of asthmatic patients in Hong Kong have gastroesophageal reflux disease (GERD) and this is associated with poorer asthmatic control, quality of life and physiological status [3]. Allergic rhinitis and its impact on asthma have also been reported in detail in a review article written by Bousquet and his colleagues [4].

Global Initiative for Asthma (GINA) guideline reported that special consideration are required in managing asthma in relation to gastroesophageal reflux, rhinitis, sinusitis, respiratory infections, obesity and surgery [2]. In order to improve the treatment of patients with asthma and to control disease that is the main goal of therapy, comorbidities must be taken into consideration, and it is important to treat these conditions [5].

The better asthma control means the better quality of life, therefore, we aimed to investigate the effect of gastroesophageal reflux, allergic rhinitis, sleep disorders with asthma control and quality of life in Turkish asthma patients at a major University Hospital in Istanbul.

## Material and Method

The study was approved by the Clinical Researches Ethic Committee of Istanbul University, Cerrahpaşa Medical Faculty (27/09/2010, No: 28936), informed written consent were obtained from all patients. The power analysis is calculated according to statistically meaningful minimal change in ACT and AQLQ values, and found that at least 29 patients are needed for study population.

## Study Population

All asthma patients who followed at asthma clinic of Istanbul University Cerrahpaşa Faculty of Medicine, Department of Pulmonary Diseases, from September 2010 to November 2010 were screened. Those patients who were 20-65 years of age, were invited to participate in this study. Patients were excluded from study entry if they have; 1) asthma attack in past one month, 2) diagnosis of active lung diseases except asthma, 3) diagnosis of sleep disorders, 4) acute upper respiratory tract infections, 5) uncontrolled hypothyroidism/hyperthyroidism, 6) depression, 7) pregnancy, 8) urinary system disorders, benign prostate hyperplasia, 9) using medicine for other comorbidities.

Patients who signed consent form were asked to fill in the Reflux Symptom Index (RSI), Allergic Rhinoconjunctivitis Symptom Index (ARSI), Pittsburgh Sleep Quality Index (PSQI), Asthma Control Test (ACT), and Asthma Quality of Life Questionnaires (AQLQ) under the supervision of a physician, and also spiromet-

ric parameters, smoking habits, height-weight ratios of cases were recorded.

**Pulmonary Function test:** Lung function tests were performed at the pulmonary function laboratory of Istanbul University Cerrahpaşa Medical Faculty, Pulmonology Department by using a ZAN 100 Spiromed (ZAN, Oberthulba, Germany), in accordance with the manufacturer's instructions. The maximum forced expiratory volume in 1 second (FEV<sub>1</sub>) was calculated from up to three technically acceptable blows in accordance with the American Thoracic Society criteria for reproducibility [7].

**Asthma Control Test (ACT):** The ACT survey is a patient-completed questionnaire with 5 items assessing asthma symptoms (daytime and nocturnal), use of rescue medication, and the effect of asthma on daily activities. Each item includes 5 response options corresponding to a 5-point Likert-type rating scale. In scoring the ACT survey responses for each of the 5 items are summed to yield a score ranging from 5 (poor control of asthma) to 25 (complete control of asthma) [8, 9]. The validated Turkish version of ACT was used [10].

**Asthma Quality of Life Questionnaire (AQLQ):** The questionnaire includes 32 questions. Patients respond to each question on a seven-point scale and recall their experiences during the previous 2 weeks. Results are expressed as four domain scores (symptoms, 12 questions; emotional function, 5 questions; activities, 11 questions; exposure to environmental stimuli, 4 questions), and as an overall score (32 questions). A change in score  $\geq 0.5$  on the seven-point scale can be considered clinically important [11-16]. The validated Turkish version of AQLQ was used [17].

**Allergic Rhinoconjunctivitis Symptom Index (ARSI):** ARSI was a self-recorded questionnaire, includes 12 questions related with eye, nose, throat and general symptoms of rhinoconjunctivitis, questions were modified and translated in Turkish from study of Wassefallen et al [18]. The severity of symptoms was assessed with reference to the previous 2 weeks, and scored on a scale from 0-4 (0=none, 1=mild, 2=moderate, 3=severe, 4=very severe). The time to complete the questionnaire was on average 5 minutes.

**Reflux Symptom Index (RSI):** RSI is a self-administered questionnaire, includes 9 questions related with laryngopharyngeal reflux. Each of the items is scored from 0 (no problem) to 5 (severe problem) [19-21].

**Pittsburgh Sleep Quality Index (PSQI):** Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. Nineteen individual items generate seven "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of scores for these seven components yields one global score. A global PSQI score greater than 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% ( $\kappa = 0.75$ ,  $p < 0.001$ ) in distinguishing good and poor sleepers [22, 23]. The validated Turkish version of PSQI was used [24].

**Body Mass Index (BMI):** Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m<sup>2</sup>) Table 1 [25].

## Results

Total of 50 patients, 16 (32%) male, 34 (68%) female who

Table 1. The International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI( kg/m <sup>2</sup> )
Underweight	<18.50
Normal range	18.50-24.99
Overweight	≥25.00
Pre-obese	25.00-29.99
Obese	≥30.00
Obese class 1	30.00-34.99
Obese class 2	35.00-39.99
Obese class 3	≥ 40.00

were followed with a diagnosis of asthma (20% intermittent, 40% mild persistent, 32% moderate persistent, and 8% severe persistent) were enrolled in this study. The mean age was 42.20±14.02 years, 23 (46%) patients had reflux symptoms, 40 (80%) had rhinitis symptoms, and 14 (28%) had comorbidities like diabetes mellitus, hypertension, renal failure. Preobesity and obesity were present in 68% of patients. The minimum, maximum, mean and standart deviation value of age, AQLQ, ACT, PSQI, ARSI, RSI and FEV1% are shown in Table 2.

There were no relation between presence of comorbidities like obesity, diabetes mellitus, hypertension, renal failure, smoking

Table 2. Age, AQLQ, ACT, PSQI, ARSI, RSI and FEV1% values

	Minimum	Maximum	Mean	SD
Age	18	68	42.20	14.02
AQLQ	51	197	123.64	35.07
ACT	5	25	16.64	5.26
PSQI	0	16	6.04	3.02
ARSI	0	48	17.48	12.51
RSI	0	36	11.26	9.73
FEV1%	38	117	85.30	17.28

history, according to ACT and AQLQ ( $p>0.05$ ).

According to ACT scores; 2 (4%) cases were completely controlled (score 25), 16 (32%) cases were partly controlled (score: 24-20), 32 (64%) cases were not controlled. Also, 30 patients had FEV1 value ≥80%, 16 had FEV1 between 60% and 80%, 4 had FEV1 <60%. There was no relationship between FEV1 value and ACT scores ( $r=0.176$ ;  $p=0.220$ ).

PSQI score was ≤5 in 26 (52%) cases, 6-9 in 20 (40%) cases and ≥10 in 4 (8%) cases.

RSI was >13 in 24 (48%) cases. The mean ARSI score was 17.48 ±12.51.

In AQLQ; The mean total score was 123.64±35.07, symptoms score was 52.69 ±16.58, activity restriction score was 41.19±12.19, emotional function score was 20.90±7.56, environmental factors score was 10.93±6.72.

Negative correlation was found between AQLQ and RSI ( $r=-0,551$ ;  $p<0.001$ ), also between AQLQ and ARSI ( $r=-0,390$ ;  $p<0.005$ ). There was no relationship between AQLQ and PSQI ( $p=0.082$ ), also there was no relationship between FEV1 value

and ACT, AQLQ, RSI, ARSI, PSQI.

Negative correlation was found between the ACT and RSI ( $r = -0.314$ ,  $p = 0.026$ ), ACT and PSQI ( $r=-0,620$ ;  $p<0.001$ ). Positive correlation was found between ACT and AQLQ. There was no relationship between ACT and ARSI ( $p=0,25$ ). All correlation analysis is shown in Table 3.

## Discussion

There was negative correlation between AQLQ and RSI , and

Tablo 3. Correlation analysis between all parameters

	RSI		ACT		PSQI		FEV1%	
	r	p	r	p	r	p	r	p
AQLQ	-,551	,000***	,667	,000***	-,249	,082	,127	,380
Symp-toms	-,542	,000***	,686	,000***	-,277	,051	,155	,283
Activity restriction	-,431	,002**	,527	,000***	-,199	,167	,160	,267
Emotional function	-,471	,001**	,672	,000***	-,357	,011*	-,028	,845
Environmental factors	-,361	,010*	,238	,096	,082	,569	,063	,664
ACT	-,314	,026*						
PSQI	,240	,093	-,620	,000***				
FEV1%	-,007	,961	,176	,220	-,112	,437		

between ACT and RSI. These results are in accordance with the recent studies [3, 5]. Cheung and his colleagues showed that, a significant proportion of asthmatic patients in Hong Kong have gastroesophageal reflux disease (GERD), and this is associated with poorer asthmatic control, quality of life, and psychological status [3]. In another study, Bisaccioni and his colleagues analyzed the data that obtained from electronic medical records of patients with severe asthma between 2006 and 2008; and they reported that 70.6 % of all severe asthma patients have GER symptoms [5]. These results were not surprise, at the beginning of 19's century, Sir William Osler formally recognized GERD as a potential trigger of asthma and stated that "...attacks may be due to direct irritation of the bronchial mucosa or indirectly, too, by reflex influences from stomach..."[26]. When time is going on, some studies supported the association between asthma and gastroesophageal reflux [3, 5, 27-29]. Also, recent studies showed the effectiveness of GERD treatment for improvements in asthma outcomes [30, 31]. However, a meta-analysis of the effectiveness of GERD treatment in patients with asthma reported that improvements in asthma outcomes were inconclusive [32]. Therefore, further studies are needed about effectiveness of GERD treatment and asthma outcomes.

The majority of patients with asthma have a history or evidence of rhinitis and up to 30% of patients with persistent rhinitis have or develop asthma [2, 33-35]. Rhinitis and asthma share several risk factors [2]. For these reasons, the Allergic Rhinitis and its Impact on Asthma (ARIA) initiative recommends that the presence of asthma must be considered in all patients with rhinitis, and that in planning treatment , both should be considered together [36, 37]. The recent studies reported that, 75-91% of all asthma patients had also rhinitis symptoms [33, 38, 39]. In our study, 80% of all asthma patients had rhinitis symptoms,

and negative correlation was found between AQLQ and ARSI ( $r = -0,390$ ;  $p < 0,005$ ). This result is similar with study of Dan Lu and his colleagues [40]. They reported that, the quality of life of patient with persistent allergic rhinitis is worse than patients with intermittent allergic rhinitis. In addition to this, we found that there was no relationship between ACT and ARSI ( $p = 0,25$ ), there is limited data in literatures so more studies are needed to conclude.

Recent studies reported that, asthma is more difficult to control in the obese patient [41-43], since different type of airway inflammation, obesity related comorbidities such as obstructive sleep apnea [2]. Luyster and his colleagues showed that, poor sleep quality is associated with poor asthma control and quality of life among asthmatics [44]. Similar to Luyster's result, in our study we found that there was negative correlation between ACT and PSQI ( $r = -0,620$ ;  $p < 0,001$ ). Nevertheless, in our study, there was no relation between obesity and ACT and AQLQ ( $p > 0,05$ ), and there was no relation between AQLQ and PSQI ( $p = 0,082$ ).

Our study has some limitations like low number of study population and absence of control group, short follow up period.

In conclusion, gastroesophageal reflux and allergic rhinoconjunctivitis negatively effect the quality of life and asthma control in asthmatic patients, also poor sleep quality is associated with poor asthma control. The diagnosis and the treatment of gastroesophageal reflux, allergic rhinoconjunctivitis and having good sleep quality are important for the success of asthma treatment. Further, detailed studies are needed to conclude.

### Competing interests

The authors declare that they have no competing interests.

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