

# Factors affecting the hospitalization of female patients with asthma

## Astımlı kadın hastaların hastaneye yatışlarını etkileyen faktörler

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### Abstract

**Aim:** Asthma is one of the most common chronic respiratory diseases and an important public health problem leading to mortality. The aim of this study was to evaluate the hospitalization rates of female patients with asthma.

**Methods:** This cross-sectional study was conducted with the approval of a university hospital ethics committee between September 2018 and January 2019. The study included a total of 183 females: 56 patients with exacerbation were included in Group 1 and 127 patients with stable asthma constituted Group 2. Demographic data, pulmonary function test results, number of hospital admissions, hospitalization rates and laboratory findings were evaluated. All statistical calculations were performed with SPSS 23 for Windows.

**Results:** The mean age, number of hospitalizations and admissions to the emergency room were significantly higher in Group 1 ( $P=0.003$ ,  $P<0.001$  and  $P<0.001$ , respectively). Patients in Group 1 had lower oxygen saturations, FEV1, FVC, FEV1/FVC values, higher respiratory and heart rates, blood glucose, lactate dehydrogenase, c-reactive protein, lactate, phosphorus, high-density lipoprotein, calcium levels, white blood cell and neutrophil counts. Increased eosinophil count and decreased basophil count were associated with increased emergency room admission rates ( $P=0.043$ ).

**Conclusion:** Women admitted to the hospital with asthma exacerbation were older and had an increased number of hospitalization rates. Higher eosinophil blood levels were associated with recurrent hospital admissions.

**Keywords:** Asthma, Hospitalization, Female

### Öz

**Amaç:** Astım en yaygın kronik solunum hastalıklarından biridir ve mortaliteye yol açan önemli bir halk sağlığı problemidir. Bu çalışmanın amacı astımlı kadın hastaların hastaneye yatış oranlarını değerlendirmektir.

**Yöntemler:** Bu kesitsel çalışma bir üniversite hastanesi etik kurulundan onay alınarak Eylül 2018 ve Ocak 2019 tarihleri arasında yapıldı. Çalışmaya 183 kadın hasta dahil edildi (alevlenme olan 56 hasta Grup 1 ve stabil astım olan 127 hasta Grup 2 olarak adlandırıldı). Demografik özellikler, akciğer fonksiyon testleri, hastaneye başvuru sayıları, hastaneye yatış oranları ve laboratuvar bulguları değerlendirildi. Tüm istatistik hesaplamaları SPSS 23 Windows ile yapıldı.

**Bulgular:** Grup 1'deki hastaların ortalama yaşı daha büyüktü ( $P=0,003$ ). Grup 1'de hastaneye yatış ve acil servise başvuru sayıları önemli derecede yüksekti ( $P<0,001$ ). Grup 1'deki hastalar daha düşük oksijen saturasyonu, FEV1, FVC, FEV1/FVC'ye ve daha yüksek solunum sayısı ve kalp atım sayısına sahipti. Bu grupta, hastalar daha yüksek kan glukozu, beyaz küre, nötrofil sayısına ve daha düşük fosfor, yüksek dansiteli lipoprotein ve kalsiyum düzeylerine sahipti. Artmış eozinofil sayısı ve azalmış bazofil sayısı acil servis başvuru oranları ile ilişkili idi ( $P=0,043$ ).

**Sonuç:** Sonuç olarak, astım alevlenme ile hastaneye başvuran kadınlar daha yaşlıydı ve hastaneye yatış oranları daha fazlaydı. Yüksek eozinofil kan seviyeleri tekrarlayan hastaneye başvurular ile ilişkilidir.

**Anahtar kelimeler:** Astım, Hastaneye yatış, Kadın

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## Introduction

Asthma is one of the most prevalent chronic airway diseases and an important public health problem leading to morbidity, mortality, and worsened quality of life globally, affecting people of all genders, ethnicities, and ages [1]. Nowadays, around 300 million people suffer from asthma disease in the world and asthma is responsible for 180.000 deaths per year, with a prevalence rate higher than 10% [2].

The incidence, prevalence, severity, and hospitalization rates of asthma vary with gender. The disease is more severe, and exacerbation rates, hospital admissions, hospitalization rates, morbidity and mortality rates are higher among women. The reasons for gender inequality may be linked to hormonal and immunological factors, as well as environmental and occupational exposures [3].

Asthma-related hospitalization rates differ among countries, genders and age groups [2]. Asthma is more common among women, and therefore it is estimated that women have higher rates of hospital admission. The main purpose of this study was to evaluate the hospitalization rates of female patients with asthma, determine the patients' demographic profile and analyze blood parameters.

## Materials and methods

### Design and assessment

This cross-sectional study was conducted with the approval of Kafkas University ethics committee, between September 2018 and January 2019 in Kars, Turkey. It included randomly selected 56 asthma patients with acute exacerbation who were referred to the emergency room (ER) (Group 1) and 127 stable asthma patients who were admitted to the Pulmonology department (Group 2) ( $n_{\text{total}}=183$ ). Group 2 patients were stable with no acute exacerbation of the disease for at least one month prior to admission and they were receiving regular treatment. Age, smoking status (smoker, ex-smoker, never a smoker), exposure to passive smoke, type of asthma (allergic, non-allergic), occupation, educational status, comorbidity, pulmonary function tests, number of hospitalizations in Pulmonology Clinic (NHPC), number of admissions to emergency room (NAER) and number of hospitalizations in the intensive care unit (NHIC) within the last year due to asthma and complications, respiratory rate, oxygen saturation in room air (%), pulse rate per minute, complete blood counts, blood gas analysis, renal-liver function tests, lipid profile, electrolytes, blood glucose and vitamin D level of patients were evaluated. According to Global Strategy for Asthma Management and Prevention 2018 report, the NAER and NHPC of Group 2 patients were not considered as asthma exacerbation. Pulmonary function tests were measured at baseline using a spirometer (Spirolab III-MIR, Italy).

### Blood samples

An alcohol swab was used to clean the skin and a band was used to tie for arm of patients. All blood samples were drawn from the veins in the forearm and collected into separate tubes with ethylenediamine tetraacetic acid (EDTA) and acid citrate dextrose. The samples were analyzed with Pentra DF Nexus, Horiba Medical, Japan with Automated Cell Counter

Methodology and Cobas C 702 Module, Roche, Switzerland. The complete blood count samples, which were stable for 24 hours at room temperature, and 36 hours at 2 – 8 °C, were stabilized optimally when run within in 4 hours of collection. The tube with acid citrate dextrose was centrifuged for 8-10 minutes at 3500-4000 revolution per minute (rpm) and serum, which remained stable for 8 hours at 2 – 8 °C, was separated.

### Statistical analysis

All statistical calculations were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, SA). All continuous variables were expressed as mean (standard deviation), and categoric variables were defined as percentages (%). The categorical parameters were compared with Chi Square test and Fischer's exact test. The normal distribution was determined by histogram and Kolmogorov-Smirnov test. Mean values of continuous variables were compared between the groups using Mann-Whitney U test. The statistical significance level was  $P<0.05$ . The power of the test was calculated with  $P_{005}$  (power analysis) program. A sample size of 86 people, 43 in each group, was needed for 80% power and 0.05 type-1 error at 95% confidence interval.

## Results

Clinical features, number of hospitalizations and referrals, respiratory findings and blood parameters of all patients included in this study are presented in **Table 1**. The mean age of the patients in Group 1 was higher than that of Group 2 ( $P=0.003$ ). Smoking status, type of asthma, occupation, educational status and comorbidities did not differ between the two groups.

The NHPC and NAER rates within the last year due to asthma and its complications in Group 1 patients were significantly higher than that of Group 2 ( $P<0.001$ ). None of the patients in Group 2 were hospitalized in the intensive care unit during the last year for asthma and its complications. Patients in Group 1 had lower oxygen saturations, FEV1, FVC, FEV1/FVC values, higher respiratory and heart rates, blood glucose, lactate dehydrogenase, c-reactive protein, lactate, phosphorus, high-density lipoprotein, calcium levels, white blood cell and neutrophil counts. Patients in Group 2 had higher red cell distribution width (RDW) and lower albumin, protein and plateletcrit (PCT) values. Eosinophil count increased, and basophil count decreased with increasing number of ER admissions ( $P=0.043$  and  $P=0.043$ , respectively). Clinical features, number of hospitalizations and admissions, respiratory findings, and blood parameters of the two groups are presented in Table 1.

Table 1: Clinical features, number of hospitalizations and admissions, respiratory findings, blood parameters of two groups

	Group 1 mean(SD) / n (%)	Group 2 mean(SD) / n (%)	P-value
Age	51.1(14.2)	44.8(12.3)	0.003
Smoking status			
Ex-smoker	8 (14.3%)	23 (18.4%)	0.399
Smoker	9 (16.1%)	24 (19.2%)	
Never smoker	39 (69.6%)	77 (61.6%)	
Exposure to passive smoke	-	1 (0.8%)	
Type of asthma			
Allergic	28 (50.9%)	52 (41.9%)	0.328
Non allergic	27 (49.1%)	72 (58.1%)	
Occupation			
Housewife	49 (87.5%)	113 (89%)	0.246
University staff	-	1 (0.8%)	
Student	-	6 (4.7%)	
Engineer	-	1 (0.8%)	
Worker	3 (5.4%)	1 (0.8%)	
Teacher	1 (1.8%)	3 (2.4%)	
Officer	3 (5.4%)	2 (1.6%)	
Educational status			
Illiterate	22 (39.3%)	39 (30.7%)	0.209
Primary school graduate	20 (35.7%)	58 (45.7%)	
Secondary school graduate	9 (16.1%)	8 (6.3%)	
High school graduate	3 (5.4%)	6 (4.7%)	
University graduate	2 (3.6%)	16 (12.6%)	
Comorbidity			
Hypertension	13 (23.2%)	25 (19.7%)	0.693
Diabetes Mellitus	4 (7.1%)	7 (5.5%)	0.739
Hyperlipidemia	2 (3.6%)	4 (3.1%)	0.596
Panic disorder	-	1 (0.8%)	0.694
Coronary Artery Disease	2 (3.6%)	5 (3.9%)	0.634
Hypothyroidism	1 (1.8%)	3 (2.4%)	0.641
Depression	1 (1.8%)	3 (2.4%)	0.641
Number of hospitalizations in Pulmonology Department (NHPC) in the last year due to asthma and complications			
None	43 (76.8%)	122 (96.1%)	<0.001
One time	8 (14.3%)	2 (1.6%)	
Two times or more	5 (8.9%)	3 (2.4%)	
Number of admissions to emergency room (NAER) in the last year due to asthma and complications			
None	29 (51.8%)	96 (75.6%)	<0.001
One time	7 (12.5%)	17 (13.4%)	
Two times	10 (17.9%)	12 (9.4%)	
Three times	5 (8.9%)	-	
Four times or more	5 (8.9%)	2 (1.6%)	
Number of hospitalizations in intensive care unit (NHIC) in the last year due to asthma and complications			
None	52 (92.9%)	127 (100%)	0.003
Once	1 (1.8%)	-	
Two times or more	3 (5.4%)	-	
Respiratory findings			
Oxygen saturation (%)	89.1(9)	94.5(2.2)	<0.001
Respiratory rate (rpm)	19.9(2.5)	15.8(1.1)	<0.001
Heart rate (rpm)	99.2(17.9)	88(10.4)	<0.001
FEV1, L	2.43(0.45)	2.65(0.46)	0.005
FVC, L	2.97(0.49)	3.15(0.52)	0.045
FEV1/FVC, %	79.8(2.8)	81(2.6)	0.006
Biochemical parameters			
Glucose, mg/dL	116.7(64.4)	104.8(44.7)	0.001
Blood Urea Nitrogen, mg/dL	31.5(17.4)	28.4(8.6)	0.658
Creatinine, mg/dL	0.7(0.22)	0.88(2.82)	0.120
Uric acid, mg/dL	4.52(1.33)	4.23(1.19)	0.209
Phosphore, mg/dL	3.39(0.6)	3.6(0.57)	0.029
Aspartate aminotransferase, U/L	19.5(6.9)	18.6(5.4)	0.552
Alanine aminotransferase, U/L	18.3(8.1)	16.8(8.9)	0.170
Lactate dehydrogenase, U/L	244.4(75.7)	210.6(45.2)	0.001
Albumin, g/dL	24.4(19.57)	13.02(16.33)	0.014
Protein, g/dL	41.44(33.39)	21.76(27.42)	0.002
Triglyceride, mg/dL	127.2(76)	125.4(71.2)	0.817
High density lipoprotein, mg/dL	50.5(15.9)	56.1(13.8)	0.009
C-reactive protein, mg/dL	11.65(27.27)	2.12(4.98)	<0.001
Very low density lipoprotein	25.1(15.1)	25.2(14.1)	0.638
Calcium, mg/dL	9.36(0.42)	9.51(0.38)	0.024
Sodium, mmol/L	139(3)	137.4(17)	0.470
Potassium, mmol/L	4.38(0.34)	4.32(0.49)	0.094
Magnesium, mg/dL	1.98(0.2)	1.93(0.15)	0.132
Vitamin D	12.94(6.21)	13.2(5.56)	0.688
Blood gas analysis			
pH	7.39(0.03)	7.39(0.02)	0.831
pCO2, mmHg	42.7(6.8)	45.1(30.8)	0.972
pO2, mmHg	33.1(12.8)	33(15)	0.787
HCO3, mmol/L	24.5(2.3)	24(1.8)	0.327
Lactate, mmol/L	1.3(0.5)	1.12(0.43)	0.013
Complete blood count			
White blood cell, 10 <sup>3</sup> /mm <sup>3</sup>	9.3(3.5)	7.8(2.2)	0.011
Hemoglobin, g/dL	14.31(1.5)	14.03(1.31)	0.078
Plateletcrit, %	0.25(0.06)	0.24(0.05)	0.409
Platelet count, 10 <sup>3</sup> /mm <sup>3</sup>	286.3(80.8)	278.4(69.4)	0.996
Red cell distribution width, %	14.8(2)	15.6(2.6)	0.023
Basophil count, 10 <sup>3</sup> /mm <sup>3</sup>	0.04(0.03)	0.04(0.03)	0.289
Eosinophil count, 10 <sup>3</sup> /mm <sup>3</sup>	0.29(0.29)	0.22(0.2)	0.640
Neutrophil count, 10 <sup>3</sup> /mm <sup>3</sup>	6.98(6.67)	4.75(1.74)	0.002
Lymphocyte count, 10 <sup>3</sup> /mm <sup>3</sup>	3.26(5.37)	2.53(3)	0.924

SD: Standard deviation

## Discussion

Asthma exacerbation is characterized by the progression of symptoms such as shortness of breath, cough, wheezing or chest tightness and decreasing lung functions [4]. This study found that higher age was associated with exacerbation in female patients with asthma. Kang et al. [5] also reported that the risk of

exacerbation was associated with age older than 45 years in mild and moderate asthma. In the study of Sekiya et al. [6] the mean age of inpatients with severe asthma was similar to that of Group 1 in our study. Asthma is a chronic inflammatory disease which is related to age and characterized by unregulated inflammation with low-grade, chronic and systemic response that causes aging [1, 7]. The aging of patients can be a risk factor for inflamed exacerbation episodes.

An asthma exacerbation episode comprises worsening of respiratory symptoms, decreased lung function tests that requires systemic steroid treatment, increased ER visits and hospitalization rates [8]. As expected in the study, patients with exacerbation had higher NHMRS, NAER, NHIC, respiratory and heart rates, lower oxygen saturations and pulmonary function tests.

In this study, we observed that patients with exacerbation had higher blood glucose, LDH, CRP, lactate levels, WBC and neutrophil counts, and lower serum phosphorus, HDL, and calcium levels. The increase in eosinophil count and decrease in basophil count during the exacerbation episode were associated with increasing number of ER admissions. Increased or decreased serum biomarker levels during this period may be due to drug side effects or inflammatory status. The association of eosinophil count with recurrent admissions may provide information regarding prognosis. Steroid therapy, used in asthma attacks, is hyperglycemic. Stress hormones such as catecholamines and cortisol may also induce hyperglycemia [9]. CRP, WBC and neutrophil counts are well-known airway-blood inflammatory and infection markers commonly used by physicians in clinical practice [10-12]. Corticosteroid therapy may cause corticosteroid-induced neutrophilic leukocytosis [13]. Beta-agonist agents used for asthma act by decreasing intracellular free Ca<sup>+</sup> ion concentration, thus relaxing smooth muscle, which may cause hypocalcemia [14]. In addition, short-acting beta agonists may decrease blood phosphate and increase lactic acid levels [13].

LDH, an intracellular cytoplasmic enzyme, is indicative of cellular integrity. The inflammatory cells are derived from LDH and the increment of LDH is related to vascular permeability and epithelial tissue necrosis. During the acute period, it is expected to increase with inflammation [15]. Surfactant is a lipid-protein composite that reduces surface tension and alveolar distance, thus effecting respiratory immune response. Low density lipoproteins induce surfactant lipid synthesis, and the composition and function of surfactant can be damaged with inflammatory diseases such as asthma. Similar to this study, it was reported that LDH and HDL levels increased during an asthma attack [15].

Severe eosinophilic asthma or eosinophilic refractory asthma is a common phenotype of asthma disease. Higher blood eosinophil count is a well-established risk factor for asthma exacerbation episodes and eosinophil count may decrease after inhaled steroid treatment [16]. Some studies demonstrated that blood eosinophil count is a substantial indicator of economic burden, management and hospitalization rates for asthma [17, 18]. Basophil cells are activated by IgE and responsible for aggravation of inflammation by releasing histamine and

leukotriene C4, but the exact function of basophils in the pathogenesis of asthma remains a myth [19].

### Limitations

This cross-sectional study, comparing women with asthma in acute and stable periods, was designed with the information obtained from the file records of the patients. The retrospective nature, lack of more specific biomarkers of inflammation, lack of mortality data and the short follow up period were the limitations of our study. More studies including these parameters are needed in the future.

### Conclusion

In conclusion, women admitted to hospital with asthma exacerbation were older and had increased number of hospitalization rates. Higher eosinophil blood levels were associated with recurrent hospital admissions.

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