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TITLE:

Association between blood eosinophil count with asthma hospital readmissions.

SHORT TITLE:

Blood eosinophil count and asthma hospital readmissions.

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ABSTRACT:

INTRODUCTION:

The presence of eosinophils in asthma inflammation is a relevant factor in the pathophysiology of the disease, however the relationship between the blood eosinophil count (BEC) with asthma severity and prognosis is still under debate.

The aim of this work is to analyze the relationship between the BEC levels and hospital readmissions in patients with asthma.

MATERIAL AND METHODS:

A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. The personal characteristics and the asthma personal history of each patient were recorded. The BEC was determined from the first blood sample taken from the patient after their arrival at the hospital. Hospital early, late and frequent readmissions were analyzed using 4 cut-off points; less than 150 eosinophils/µL vs ≥150/µL, less than 200 vs v200 /µL, less than 300 vs ≥300/µL, and less than 400 vs ≥400/µL.

RESULTS:

We have included 1,316 patientsy, 70% of whom are women, as well as a mean age of 60 years, and a mean FEV1 of 73.5% of the reference value. The mean eosinophil blood count was 201.7 cells/µL. A BEC ≥300 cells/µL showed a reduction of risk of late readmission of 42%, a BEC ≥400 cells/µL showed a reduction in late readmission risk of 41% and decrease in frequent late readmission of 63%.

CONCLUSIONS:

Our study appears to support that an elevated BEC is associated with a lower incidence of asthma hospital readmissions.

KEY WORDS: Asthma; Eosinophils; Hospital admissions; Readmissions; Prognosis; Severity.

INTRODUCTION:

Asthma is a heterogeneous disease in which the pathophysiology interacts with genetic and environmental factors (1). The presence of eosinophils in asthma inflammation has been known for many years to be a relevant factor in the pathophysiology of the disease (2), and has demonstrated its use as a biomarker in the identification of patients with an improved response to some treatments (3,4).

It has been known since the end of the 1950's that the sputum eosinophil count (SEC) is a predictor of the response to treatment with corticosteroids (5). However, eosinophils are not a marker of severity in all asthmatic patients. Thus, when Wenzel et al, analyzed the bronchial biopsies of patients with severe asthma refractory to corticosteroids, they observed eosinophilia in approximately half of these patients, while in the rest the presence of eosinophils was very limited (6).

Since then, interesting studies have been carried out to determine the usefulness of eosinophils in the management of asthma, but the controversy persists.

The studies available seem to support that the SEC levels are associated with more severe asthma or with a poorer outcome of the disease (7,8,9,10)

However, the data on the blood eosinophil count (BEC) are more discrepant. Thus, some authors report that the BEC do not correlate with the severity of the asthma (7,8), while other authors observed that the patients with a high BEC have more severe asthma (11,12); or on the contrary, patients with a high BEC are associated with less severe exacerbations (13).

The greater usefulness of SEC levels has not been reflected in all the studies, since in one recent publication, on analyzing the response to mepolizumab in severe eosinophilic asthma, it was observed that the BEC was a better predictor of response than the SEC (14)

On the other hand, the determination of SEC is a particularly complex technique and of high cost. Thus, it is not available in all health centers, as such that other methods have been explored for identifying the eosinophilic phenotype, such as the determination of the fraction of exhaled nitric oxide, periostin levels in serum, or the BEC (15).

Given that the BEC determination is widely available, and is cheaper than the sputum analysis, it could be used as a more effective indicator in the management of asthma.

Hospital admissions account for a significant part of the health care costs of asthma, as well having a high impact on the quality of life of the patients and their families (16,17,18). In Spain, a slight downward trend is observed in the mortality due to asthma (19), although hospital admissions continue to increase, particularly in elderly women (20).

Hospital readmissions may be a good indicator of the quality of the health care, as well as a potential target for reducing health care costs (21,22,23)

The aim of this work is to analyze the relationship between the BEC levels and hospital readmissions in patients with asthma.

MATERIAL and METHODS:

A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. The data were gathered by two members of the research team whilst reviewing the clinical records. In cases where there were discrepancies in the evaluation of any data, the decision was made by consensus with the rest of the group members. The definition of asthma exacerbation was based on the discharge report produced by the specialist doctor who treated the patients (pulmonlogists or internists), with review of medical records by our research team (including pulmonologists, internists, and radiologists).

Cases where the reason was due to another specific cause, such as pulmonary embolism or pneumonia, were excluded.

The personal characteristics of each patient were recorded including age (categorized into 4 groups: from 18 to 35 years, from 36 to 55 years, from 56 to 75 years, and greater than 75 years), gender, body mass index (BMI), classifying the patients into normal weight when they had a BMI less than 25 kg/m2, as overweight with a BMI greater than or equal to 25, and a BMI greater than or equal to 30 as obese (24). Comorbidity was evaluated according to the Charlson index (25), and smoking classified as active smokers, ex-smokers, or never smoked.

An analysis was performed on the asthma personal history, including the baseline treatment, lung function based on the forced expiratory volume (FEV1) as a percentage of the reference value, the baseline severity of the asthma according to the Global Initiative for Asthma (GINA) 2006 criteria (26), having had any hospital emergency department (ED) visits or admissions due to asthma in the previous year. As regards the exacerbation index, the duration of hospital stay was analyzed (including from the time the patient arrived in the ED until discharge), and treatment after hospital discharge.

Previous year emergencies were stratified into 3 groups, one group with those who did not make any visit to the ED in the previous year, another that made one to three visits, and a last group that made four or more visits to the ED in the previous year. Previous year hospital admissions were stratified into 3 groups, one group with those who did not have any hospital admission in the previous year, another that had one hospital admission, and a last group that had two or more hospital admissions in the previous year

The BEC was determined from the first blood sample taken from the patient after their arrival at the hospital. Hospital readmissions were analyzed using 4 cut-off points; less than 150 eosinophils/µL vs ≥150/µL, less than 200 vs v200 /µL, less than 300 vs ≥300/µL, and less than 400 vs ≥400/µL. (9,12,27,28)

An early readmission (ER) was defined as that which occurred in the following 15 days after hospital discharge, and late readmission (LR) as that occurring from 16 days after discharge (22). In order to analyses the LR, those that had no LR were compared with those that had any LR. For the evaluation of the relationship with the patients frequent late readmissions (FLR), those that had no LR were compared with those that had had two or more LR during the study period.

The hospital stay included from the time the patient arrived in the ED until discharge.

The Review Board on Human Studies at our institution approved the protocol (**Register Code**: 2017/093).

STATISTICAL ANALYSIS:

The data were tested for normal distribution using the Kolmogorov-Smirnov test. The comparison of the categorical variables was performed using the Chi-squared test.

The variables with significant differences in the univariate analysis were included in the multivariate analysis using logistic regression. The Odds Ratios (OR) of a higher incidence of ER and LR were calculated using a binary logistic regression, including blood eosinophil count, gender, and treatment after hospital discharge with combinations of inhaled corticosteroids and long acting beta-agonists (ICS-LABA), inhaled, or oral corticosteroids, as independent variables.

All statistical analyses were performed using SPSS 15.0 for Windows, Version 15.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS:

We have included 1,316 patients in our study, 70% of whom are women, as well as a mean age of 60 years, and a mean FEV1 of 73.5% of the reference value. The mean eosinophil blood count was 201.7 cells/µL (Table 1). The main characteristics of included patients according to the BEC are shown in table 2.

Readmission data were collected from 1,170 patients. Of these, there was early readmission (ER) in 17 (1.4%) patients, a late readmission (LR) in 241 (21%) patients, and two or more late readmissions in 74 (6%) patients (Table 3).

A BEC of 400 or more cells/µL was found in 16% of the patients, with 23% with 300 or more cells/µL (Table 3).

On analyzing the correlation between the different BEC levels in which the sample was stratified with the ER, we did not observe any significant relationship. A lower incidence of LR was observed in patients with a BEC greater than 300 cells/µL or 400 cells/µL, as well as an FLR with a BEC greater than 400 cells/µL (table 3).

In the multivariate analysis it was confirmed that a BEC ≥300 cells/µL showed a reduction of risk of LR of 42%, a BEC ≥400 cells/µL showed a reduction in LR risk of 41% and decrease in FLR of 63% (Table 4)

DISCUSSION:

The results of our study show that more elevated levels of BEC are predictors of a lower risk of LR. The publications available in the literature that analyses the relationship between the BEC and asthma show differing results. Pola-Bibian et al, in a recent publication with patients from a Spanish hospital obtained results similar to ours, with a lower rate of hospital admissions after an exacerbation due to asthma in patients with a higher BEC (13). Other authors obtained the opposite results, with more exacerbations in the patients with a higher BEC (11,12,27); and in other cases no relationship was found between the BEC and exacerbations (9,28) or with the severity of the asthma

(7,8).

The divergence between the results of the different studies, could justified, at least partly, due to the different methodologies used between them. In the first place, to consider the variability in the definitions of exacerbations used, since in our study we have included asthmatic patients who had any exacerbation requiring hospital admission, and we have used the incidence of readmissions, both ER and LR, as an indication of a worse outcome. In the study by Pola-Bibian et al, the rate of admission on the hospital ward after an exacerbation that required an ER visit is evaluated (13), whilst Tran et al and Malinovschi et al, analyzed asthma attacks or ER visits referred to in a survey by the patients themselves (27,28); and others evaluate acute attacks based on the need for systematic corticosteroids (9,11,12).

Significant differences are also observed in the size of the sample studied, between the more than 100,000 patients of the study by Price et al, and the 158 of the study by Silkoff et al (8); or in the mean age of the population studied, from 40 years in the study by Tran et al (28) up to the 60 years of our study (Table 1).

Although some authors defend the use of the BEC as a marker of severe eosinophilic asthma (14), the body compartment in which the eosinophils are evaluated is an aspect to consider, since the eosinophils in blood do not appear to have the same significance as those in sputum. Schleich et al shows us that patients with both the BEC and SEC elevated, have significantly more acute asthma attacks than if they are elevated in only one of these compartments (9). Furthermore, in the study by Silkoff et al, the SEC levels correlated with the severity of the asthma, but the BEC levels did not show any differences as regards the severity of the disease (8).

Neither is there any agreement in the literature on the correlation between the BEC and the SEC, since some authors defend that the BEC is a good predictor of the SEC (29,30), but others disagree, saying that this correlation between the BEC and SEC is weak (8,31,32). In a recent publication it was observed that approximately one third of the patients had differences between the BEC and

SEC, without being able to clarify the causes of this (9).

Another aspect under discussion is the reliability of the BEC or SEC for defining the inflammatory characteristics of a particular patient, since some authors suggest that both the BEC and the SEC show significant variation through long or short periods of time, and as such they would not be stable markers to define eosinophilia (33,34).

The prevalence of peripheral eosinophilia does not seem to be a factor that determines the difference in our results with other studies, as the proportion of patients with a BEC greater than 400 cells/µL in our population is similar to that reported by other authors, where it varies between 16% and 18% (11,12,28), although a bit lower than the 26% referred to by Schleich et al in a Belgian population (9).

One of the possible causes of this relationship between a lower BEC and more exacerbations could be due to the effect of a virus, since these are one of the main causes of acute asthma attacks (35), and it has been demonstrated that virus infections increase neutrophilic inflammation (36).

The discrepancies between different studies appear to support the need to continue studies on the correct use of the BEC in patients with asthma. The combination of different biomarkers may probably be required in order to improve the ability to identify inflammatory phenotypes, as suggested by the studies of Malinovschi et al, combining FENO and BEC, or de Schleich et al, combining BEC and SEC (9,27)

Our study has some limitations. On the one hand, on being retrospective it lacks information on some of the included variables   and on comorbidities. On the other hand, there were no spirometry data in more than a third of the patients, and for this reason the asthma diagnosis was established based on the opinion of the medical specialist that attended to the patient. This seems reasonable, as shown in a recent Canadian study where patients admitted to hospital with a primary discharge diagnosis of asthma had a positive predictive value of 90% of being asthma-related (37). Finally, the determination of the BEC is made on a single occasion (single-point measurement), which does not take into account fluctuations in the levels of BEC in the long-term. Furthermore, the impact of BEC on asthma readmissions should be cautiously analysed considering the differences observed in some characteristics of the patients with high or low levels of BEC, similar to the data presented by other authors (9, 11, 12), which could have some impact on the results,

In conclusion, the results of our study appear to support that an elevated BEC is associated with a lower incidence of future acute asthma attacks in patients with asthma that required a previous hospital admission.

References

1. http://ginasthma.org/2017-gina-report-global-strategy-for-asthma-management-and-prevention/ Accessed 20 Aug 2017.
2. Denlinger LC, Phillips BR, Ramratnam S, et al. Inflammatory and Comorbid Features of Patients with Severe Asthma and Frequent Exacerbations. Am J Respir Crit Care Med. 2017 Feb 1;195(3):302-313
3. Muñoz X, Bustamante V, Lopez-Campos JL et al. Usefulness of noninvasive methods for the study of bronchial inflammation in the control of patients with asthma. Int Arch Allergy Immunol. 2015;166(1):1-12
4. Albers FC[1], Müllerová H[2], Gunsoy NB[3], et al. Biologic treatment eligibility for real-world patients with severe asthma: The IDEAL study. J Asthma. 2017 Jun 16:1-9.
5. Gauthier M, Ray A, Wenzel SE. Evolving Concepts of Asthma. Am J Respir Crit Care Med. 2015 Sep 15;192(6):660-8.
6. Wenzel SE, Schwartz LB, Langmack EL, et al. Evidence that severe asthma can be divided pathologically into two inflammatory subtypes with distinct physiologic and clinical characteristics. Am J Respir Crit Care Med 1999;160:1001–1008.
7. Amelink M, de Groot JC, de Nijs SB, et al. Severe adult-onset asthma: A distinct phenotype. J Allergy Clin Immunol. 2013 Aug;132(2):336-41.
8. Silkoff PE, Strambu I, Laviolette M, et al. Asthma characteristics and biomarkers from the Airways Disease Endotyping for Personalized Therapeutics (ADEPT) longitudinal profiling study. Respir Res. 2015 Nov 17;16:142.
9. Schleich FN, Chevremont A, Paulus V et al. Importance of concomitant local and systemic eosinophilia in uncontrolled asthma. Eur Respir J. 2014 Jul;44(1):97-108.
10. Inoue H, Ito I, Niimi A, et al. CT-assessed large airway involvement and lung function decline in eosinophilic asthma: The association between induced sputum eosinophil

differential counts and airway remodeling. J Asthma. 2016 Nov;53(9):914-21

11. Price DB, Rigazio A, Campbell JD, et al. Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study. Lancet Respir Med. 2015 Nov;3(11):849-58.
12. Zeiger RS, Schatz M, Li Q, et al. High blood eosinophil count is a risk factor for future asthma exacerbations in adult persistent asthma. J Allergy Clin Immunol Pract. 2014 Nov-Dec;2(6):741-50
13. Pola-Bibian B, Dominguez-Ortega J, Vilà-Nadal G, et al. Asthma exacerbations in a tertiary hospital: clinical features, triggers, and risk factors for hospitalization. J Investig Allergol Clin Immunol. 2016 Dec 14:0.
14. Katz LE, Gleich GJ, Hartley BF, et al. Blood eosinophil count is a useful biomarker to identify patients with severe eosinophilic asthma. Ann Am Thorac Soc. 2014 May;11(4):531-6
15. Nair P.. What is an "eosinophilic phenotype" of asthma? J Allergy Clin Immunol. 2013 Jul;132(1):81-3
16. Domínguez-Ortega J, Phillips-Anglés E, Barranco P, et al. Cost-effectiveness of asthma therapy: a comprehensive review. J Asthma 2015;52(6):529-37
17. Ivanova JI, Bergman R, Birnbaum HG, Colice GL, Silverman RA, McLaurin K. Effect of asthma exacerbations on health care costs among asthmatic patients with moderate and severe persistent asthma. J Allergy Clin Immunol. 2012 May;129(5):1229-35.
18. Gonzalez Barcala FJ, La Fuente-Cid RD, Alvarez-Gil R, Tafalla M, Nuevo J, Caamaño-Isorna F. Factors associated with a higher prevalence of work disability among asthmatic patients. J Asthma. 2011 Mar;48(2):194-9.
19. Gonzalez-Barcala FJ, Aboal J, Carreira JM, et al. Trends of asthma mortality in Galicia from 1993 to 2007. J Asthma. 2012 Dec;49(10):1016-20.
20. Gonzalez-Barcala FJ, Aboal J, Valdes L, et al. Trends in adult asthma hospitalization: gender-age effect. Multidiscip Respir Med. 2011 Apr 30;6(2):82-6

21. Buyantseva LV, Brooks J, Rossi M, Lehman E, Craig TJ. Risk factors associated with 30-day asthma readmissions. J Asthma. 2016 Sep;53(7):684-90.
22. Ashton CM, Kuykendall DH, Johnson ML, Wray NP, Wu L. The association between the quality of inpatient care and early readmission. Ann Intern Med. 1995 Mar 15;122(6):415-21.
23. Moran J, Colbert CY, Song J, et al. Residents examine factors associated with 30-day, same-cause hospital readmissions on an internal medicine service. Am J Med Qual. 2013 Nov-Dec;28(6):492-501.
24. http://www.who.int/mediacentre/factsheets/fs311/en/ Accessed 15 Aug 2017.
25. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.
26. http://www.ginasthma.org/local/uploads/files/GINA_Report_072007_1.pdf. Accessed 15 Aug 2017.
27. Malinovschi A[1], Fonseca JA, Jacinto T, et al. Exhaled nitric oxide levels and blood eosinophil counts independently associate with wheeze and asthma events in National Health and Nutrition Examination Survey subjects. J Allergy Clin Immunol. 2013 Oct;132(4):821-7
28. Tran TN, Khatry DB, Ke X et al. High blood eosinophil count is associated with more frequent asthma attacks in asthma patients. Ann Allergy Asthma Immunol. 2014 Jul;113(1):19-24. Westerhof et al (erj 2015:688)
29. Zhang XY, Simpson JL, Powell H, et al. Full blood count parameters for the detection of asthma inflammatory phenotypes. Clin Exp Allergy. 2014 Sep;44(9):1137-45.
30. McGrath KW, Icitovic N, Boushey HA, et al. A large subgroup of mild-to-moderate asthma is persistently noneosinophilic. Am J Respir Crit Care Med. 2012 Mar 15;185(6):612-9.

31. Hastie AT, Moore WC, Li H, et al. Biomarker surrogates do not accurately predict sputum eosinophil and neutrophil percentages in asthmatic subjects. J Allergy Clin Immunol. 2013 Jul;132(1):72-80.

32. Spector SL[1], Tan RA. Is a single blood eosinophil count a reliable marker for "eosinophilic asthma?". J Asthma. 2012 Oct;49(8):807-10.

33. Hancox RJ[1], Cowan DC, Aldridge RE, et al. Asthma phenotypes: consistency of classification using induced sputum. Respirology. 2012 Apr;17(3):461-6.

34. Eggo RM[1], Scott JG[2], Galvani AP[3], et al. Respiratory virus transmission dynamics determine timing of asthma exacerbation peaks: Evidence from a population-level model. Proc Natl Acad Sci U S A. 2016 Feb 23;113(8):2194-9

35. Zhu J, Message SD, Qiu Y et al. Airway inflammation and illness severity in response to experimental rhinovirus infection in asthma. Chest. 2014 Jun;145(6):1219-1229

36. Canadian Institute for Health Information. CIHI data quality study of the 2005e2006 discharge abstract database. Ottawa, Ontario. 2009. https://secure.cihi.ca/free_products/DAD_DQ_study_2005_2006_August_2009_e.pdf Accessed 8 Aug 17.

Table(s)

Table 1.-Characteristics of study population

Variables	
Age, M (SD)	60.02 (20.2)
Hospital stay (days), M (SD)	12.0 (25.3)
FEV1 (precent predicted), M (SD)	73.5 (25.1)
Eosinophil count (cells/µL), M (SD)	201.7 (457.2)
Gender	
Male, N (%)	395 (30)
Female, N(%)	921 (70)
Smokers	
Never smoker, N (%)	552 (42)
Current smoker, N (%)	224 (17)
Former smoker, N (%)	129 (10)
Unknown, N (%)	411 (31)
FEV1 (percent predicted)	
≥80%, N (%)	314 (40)
≥60% to <80%, N (%)	221 (28)
<60%, N (%)	251 (32)
BMI	
Obesity, N (%)	249 (34)
Overweight, N (%)	260 (35)
Normal weight, N (%)	228 (31)
Hospital admissions previous year	
0, N (%)	1091 (83)
1, N (%)	160 (12)
≥2, N (%)	64 (5)
Emergency visits previous year	
0, N (%)	984 (75)
1-3, N (%)	301 (23)
≥4, N (%)	30 (2)
Charlson index	
0 points, N (%)	489 (37)
1 point, N (%)	438 (33)
≥2 points, N (%)	388 (30)
Asthma severity	
Intermittent, N (%)	257 (19)
Mild, N (%)	218 (17)
Moderate, N (%)	208 (16)
Severe, N (%)	266 (20)
Unclassified, N (%)	367 (28)
ICS-LABA before admission	
Yes, N (%)	419 (32)
No, N (%)	897 (68)
ICS before admission	
Yes, N (%)	232 (18)
No, N (%)	1084 (82)
OCS before admission	
Yes, N (%)	138 (10)
No, N (%)	1178 (90)
ICS-LABA at hospital discharge	

Yes, N (%)	850 (65)
No, N (%)	466 (35)
ICS at hospital discharge	
Yes, N (%)	1066 (81)
No, N (%)	250 (19)
OCS at hospital discharge	
Yes, N (%)	839 (64)
No, N (%)	477 (36)

M: mean; SD: Standard deviation; N: number on cases; BMI: Body mass index; ICS-LABA: combination inhaled corticosteroids-long acting beta agonists; ICS: inhaled corticosteroids; OCS: oral corticosteroids.

Table(s)

Table 2.-Characteristics of study population, according to blood eosinophils count

Variables	Blood eosinophils <300 per ml	Blood eosinophils ≥300 per ml	p <300 vs ≥300	Blood eosinophils <400 per ml	Blood eosinophils ≥400 per ml	p <400 vs ≥400
Age, M (SD)	63.7 (18.8)	47.7 (19.9)	0.000	62.5 (19.4)	46.3 (19.4)	0.000
FEV1 (percent predicted), M (SD)	72.3 (25.9)	79.0 (22.7)	0.001	72.6 (25.5)	80.7 (22.8)	0.001
Gender			0.000			0.000
Male, N (%)	252 (69.8)	109 (30.2)		280 (77.6)	81 (22.4)	
Female, N(%)	643 (79.7)	164 (20.3)		705 (87.4)	102 (12.6)	
Smokers			0.000			0.000
Never smoker, N (%)	364 (76.5)	112 (23.5)		403 (84.7)	73 (15.3)	
Current smoker, N (%)	122 (61.0)	78 (39.0)		147 (73.5)	53 (26.5)	
Former smoker, N (%)	101 (80.8)	24 (19.2)		107 (85.6)	18 (14.4)	
Unknown, N (%)	309 (83.7)	60 (16.3)		329 (89.2)	40 (10.8)	
FEV1 (percent predicted)			0.001			0.001
≥80%, N (%)	182 (64.8)	99 (35.2)		209 (74.4)	72 (25.6)	
≥60% to <80%, N (%)	139 (69.2)	62 (30.8)		158 (78.6)	43 (21.4)	
<60%, N (%)	169 (79.7)	43 (20.3)		187 (88.2)	25 (11.8)	
BMI			0.000			0.000
Obesity, N (%)	124 (61.4)	78 (38.6)		145 (71.8)	57 (28.2)	
Overweight, N (%)	158 (68.4)	73 (31.6)		179 (77.5)	52 (22.5)	
Normal weight, N (%)	178 (80.5)	43 (19.5)		195 (88.2)	26 (11.8)	
Charlson index			0.000			0.000
0 points, N (%)	285 (65.1)	153 (34.9)		338 (77.2)	100 (22.8)	
1 point, N (%)	317 (81.1)	74 (18.9)		341 (87.2)	50 (12.8)	
≥2 points, N (%)	294 (86.5)	46 (13.5)		307 (90.3)	33 (9.7)	
Asthma severity			0.000			0.000
Intermittent, N (%)	147 (62.0)	90 (38.0)		175 (73.8)	62 (26.2)	
Mild, N (%)	139 (72.4)	53 (27.6)		154 (80.2)	38 (19.8)	
Moderate, N (%)	131 (72.0)	51 (28.0)		146 (80.2)	36 (19.8)	
Severe, N (%)	205 (87.6)	29 (12.4)		216 (92.3)	18 (7.7)	
Unclassified, N (%)	273 (84.3)	51 (15.7)		294 (90.7)	30 (9.3)	
ICS-LABA before admission			0.018			0.015
Yes, N (%)	304 (80.9)	72 (19.1)		331 (88.0)	45 (12.0)	
No, N (%)	592 (74.6)	202 (25.4)		655 (82.5)	139 (17.5)	
ICS before admission			0.422			0.891
Yes, N (%)	167 (78.8)	45 (21.2)		178 (84.0)	34 (16.0)	
No, N (%)	729 (76.1)	229 (23.9)		808 (84.3)	150 (15.7)	
OCS before admission			0.000			0.0.34
Yes, N (%)	109 (90.1)	12 (9.9)		110 (90.9)	11 (9.1)	
No, N (%)	787 (75.0)	262 (25.0)		876 (83.5)	173 (16.5)	
ICS-LABA at hospital discharge			0.515			0.178
Yes, N (%)	589 (77.2)	174 (22.8)		651 (85.3)	112 (14.7)	
No, N (%)	307 (75.4)	100 (24.6)		335 (82.3)	72 (17.7)	
ICS at hospital discharge			0.017			0.005
Yes, N (%)	154 (70.3)	65 (29.7)		171 (78.1)	48 (21.9)	
No, N (%)	742 (78.0)	209 (22.0)		815 (85.7)	136 (14.3)	
OCS at hospital discharge			0.012			0.012
Yes, N (%)	552 (74.2)	192 (25.8)		612 (82.3)	132 (17.7)	
No, N (%)	344 (80.8)	82 (19.2)		374 (87.8)	52 (12.2)	

M: mean; SD: Standard deviation; N: number on cases; BMI: Body mass index; ICS-LABA: combination inhaled corticosteroids-long acting beta agonists; ICS: inhaled corticosteroids; OCS: oral corticosteroids.

Table(s)

Table 3.-Number of patients with early and late readmissions according to blood eosinophil count. Univariate analysis.

	Total patients, n (%)	Early readmission, n (%)		p	Late readmission, n (%)		p	Frequent late readmission, n (%)		p
		0	≥1		0	≥1		0	≥2	
		1153 (99)	17 (1)		929 (79)	241 (21)		929 (79)	74 (6)	
<150 cells/μL	770 (66)	756 (66)	14 (82)	0.199	602 (65)	168 (70)	0.170	602 (65)	53 (72)	0.256
≥150 cells/ μL	400 (34)	397 (34)	3 (18)		327 (35)	73 (30)		327 (35)	21 (28)	
<200 cells/μL	774 (66)	760 (66)	14 (82)	0.200	606 (65)	168 (70)	0.195	606 (65)	53 (72)	0.309
≥200 cells/ μL	396 (34)	393 (34)	3 (18)		323 (35)	73 (30)		323 (35)	21 (28)	
<300 cells/μL	896 (77)	881 (76)	15 (88)	0.388	**698 (75)**	**198 (82)**	**0.021**	698 (75)	63 (85)	0.065
≥300 cells/μL	274 (23)	272 (24)	2 (12)		**231 (25)**	**43 (18)**		231 (25)	11 (15)	
<400 cells/μL	986 (84)	969 (84)	17 (100)	0.091	**770 (83)**	**216 (90)**	**0.010**	**770 (83)**	**69 (93)**	**0.021**
≥400 cells/ μL	184 (16)	184 (16)	0 (0)		**159 (17)**	**25 (10)**		**159 (17)**	**5 (7)**	

Early readmission: in the following 15 days after hospital discharge (0 versus ≥1 readmissions)

Late readmission: from 16 days after discharge (0 versus ≥1 readmissions).

Frequent late readmission: from 16 days after discharge (0 versus ≥2 readmissions).

Table(s)

Table 4.- Multivariate analysis of readmissions according to blood eosinophil count.

Adjusted by gender and treatment at hospital discharge.

	OR (CI95%)
LATE READMISSION (0 versus ≥1) (Cut-point: 300 cells/μL)	
<300 cells/μL	1
≥300 cells/μL	**0.579 (0.471-0.979)**
Male	1
Female	1.160 (0.845-1.592)
ICS-LABA No	1
ICS-LABA Yes	1.249 (0.822-1.900)
ICS No	1
ICS Yes	1.107 (0.667-1.837)
OCS No	1
OCS Yes	0.814 (0.601-1.101)
LATE READMISSION (0 versus ≥1) (Cut-point: 400 cells/μL)	
<400 cells/μL	1
≥400 cells/ μL	**0.587 (0.373-0.923)**
Male	1
Female	1.149 (0.837-1.577)
ICS-LABA No	1
ICS-LABA Yes	1.241 (0.816-1.886)
ICS No	1
ICS Yes	1.111 (0.669-1.843)
OCS No	1
OCS Yes	0.817 (0.603-1.106)
FREQUENT LATE READMISSION (0 versus ≥2) (Cut-point: 400 cells/μL)	
<400 cells/μL	1
≥400 cells/ μL	**0.366 (0.144-0.929)**
Male	1
Female	0.994 (0.589-1.677)
ICS-LABA No	1
ICS-LABA Yes	1.093 (0.553-2.161)
ICS No	1
ICS Yes	0.594 (0.232-1.517)
OCS No	1
OCS Yes	1.157 (0.681-1.967)

OR: Odds Ratio; CI: Confidence interval; ICS-LABA: combination inhaled corticosteroids-long acting beta agonists; ICS: inhaled corticosteroids; OCS: oral corticosteroids.

***Conflict of Interest Statement**

CONFLICT OF INTEREST

The authors have not any conflict of interest related to this article.

HIGHLIGHTS:

The blood eosinophil count (BEC) could have some impact on asthma

The relationship between BEC and asthma prognosis is still under debate

The effect doesn´t seem to be the same in all populations.

In our population less BEC is related to more exacerbations