Assessment of neutrophil/lymphocyte percentage in bronchial asthma

Rasha M. Hendy[a], Mona A. Elawady[b], Amira I. Mansour[c]

Departments of [a]Chest Diseases, [b]Public Health, [c]Clinical and Chemical Pathology, Benha Faculty of Medicine, Benha University, Banha, Egypt

Correspondence to Rasha M. Hendy, Lecturer of chest disease, Doctorate degree, Chest Department, Benha University Hospital, Banha, Egypt. Tel: 0132530759; Mob: 01028340748; e-mail: rashahendy97@yahoo.com

Received 30 July 2018
Accepted 13 November 2018

The Egyptian Journal of Chest Diseases and Tuberculosis 2019, 68:74–79

Background
Neutrophil/lymphocyte percentage is a helpful test for evaluation of systemic inflammation. This study aimed to investigate neutrophil/lymphocyte percentage as an evidence of control status in bronchial asthma.

Patients and methods
The study included 45 (20 males and 25 females) patients and 45 apparently healthy subjects. Full clinical evaluation, complete blood count (CBC) with differential white blood cell count, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and total IgE measurement were done for participants.

Results
Neutrophil/lymphocyte percentage and CRP were higher in asthmatics than controls (statistically significant difference), and they were significantly increased with uncontrolled asthma. Neutrophil/lymphocyte percentage could predict uncontrolled asthma with a sensitivity of 66.7%, specificity of 75.6%, positive predictive value of 73.2%, negative predictive value of 69.4% and accuracy of 71.1%. Neutrophil/lymphocyte percentage increased in asthmatics with asthma control test (ACT) less than 20 versus patients with ACT of at least 20 (statistically significant difference), whereas neutrophil/lymphocyte percentage did not differ significantly among the patients with asthma regarding sex and smoking. Neutrophil/lymphocyte percentage had direct proportional relation with CRP and ACT, whereas the relations between neutrophil/lymphocyte percentage and age, eosinophils, IgE, Forced expiratory volume in first second (FEV_1%), duration of the disease, or number of attacks per year were nonsignificant. No significant correlation was found between controlled and uncontrolled cases regarding total leukocyte count (TLC), duration, and onset of the disease. The number of attacks was significantly higher in uncontrolled cases than controlled ones.

Conclusion
Neutrophil/lymphocyte percentage could predict uncontrolled asthma with high sensitivity and specificity. Neutrophil/lymphocyte percentage is a rapid, inexpensive method with routine CBC analysis and could be a useful predictor of asthma control.

Keywords:
asthma, C-reactive protein, lymphocyte, neutrophil

Egypt J Chest Dis Tuberc 68:74–79

2090-9950

Introduction

Bronchial asthma is a chronic widespread health problem all over the world. Asthma control status was clearly outlined in the last revision of the Global Initiative for Asthma (GINA) guidelines [1]. It incorporated severity of asthma, quality of life, and asthma medications in assessing control status. Access to effective treatment allows asthma to be well controlled in most patients. However, a large percentage of patients do not attain adequate asthma control despite optimal therapy. Inadequately controlled patients are at high risk of severe exacerbations and death [2]. Asthma control test (ACT) is a useful clinical method to quantify asthma control status, and it includes a questionnaire about manifestation, medications use, and personal reporting of asthma control [3].

Inflammatory cells and mediators play an important role in asthma and have numerous effects on human airways. In addition, increased circulating proinflammatory mediators like interleukin-6 and tumor necrosis factor-α have a role in mediating inflammation. These mediators also stimulate the liver to produce acute-phase proteins like C-reactive protein (CRP) [4]. An elevation in the neutrophil/lymphocyte percentage, which is a marker of inflammation, has been associated with disease severity, hospitalization, malnutrition, and mortality in other chronic diseases such as cardiovascular, chronic obstructive pulmonary disease (COPD) and kidney disorders [5].

Aim

The aim of the work is to study neutrophil/lymphocyte percentage as an inflammatory marker in asthmatics and its relation to asthma control and other parameters.

Patients and methods

The present cross-sectional study involved 45 patients with asthma recruited from the chest outpatient clinic and Inpatient Department of Benha University Hospitals, in the period from July 2016 to June 2017. Asthma diagnosis was based on GINA guidelines [1]. Moreover, 45 age-matched and sex-matched apparently healthy subjects were included as controls.

Patients with hypertension, diabetes, coronary artery disease, cancer, liver and kidney diseases, taking systemic steroids, experiencing acute asthma attack (because infection may affect neutrophil level), and having fever, cough, and sputum complaints were excluded from the study. Physical examination of all asthmatics and control groups was performed to exclude infection. Subjects with finding of infection were excluded from the study. Asthmatics involved two groups: group I (well and partially controlled patients, ACT≥20) and group II (poorly controlled, ACT<20).

All participants were subjected to full clinical evaluation (history and physical examination), complete blood count (CBC) with differential white blood cells count by automated hematology system (Sysmex XE 5000, Sysmex America, Inc., Sysmex® XE-5000 Analyzer) [6], Erythrocyte sedimentation rate (ESR) by Westergren method [7], CRP using latex agglutination (CRP-Latex cromatest) (Biotrax Testing, Cheektowaga, New York, USA), measurement of total serum IgE concentration using an ELISA immunoassay (Immunospec Corporation; ref.: E29-006, Randburg, South Africa), pulmonary function tests (spirometry), and Asthma Control Test.

ACT was done by asking patients with asthma to complete five questions according to manifestations of asthma, use of relievers, and the effect of the disease on their lives. Scores range from 5 to 25. A total score of 25 is considered as a well control, the level between 20 and 24 is a partial, control whereas a level of 19 and below is a poor control [4].

Statistical analysis

Quantitative data were assessed using mean and SD, whereas frequency and percentage were used with qualitative data. Student's *t*-test was used to compare means of different groups, but χ^2-test to compare frequencies. Correlation coefficient was used to find relation between neutrophil/lymphocyte percentage and other variables. A *P* value less than 0.05 was considered statistically significant. All statistical analysis was carried out using the computerized statistical package for the social sciences (SPSS version 20.0 for Windows; SPSS Inc., Chicago, Illinois, USA).

Results

The study included 90 subjects, where 40% of them were males and 60% were females. Their mean age was 35.44±13.0 years (18–88 years). Neutrophil/lymphocyte percentage and CRP levels were higher in asthmatic than controls (with statistically significant difference) (*P*=0.001; Table 1).

Receiver operating character (ROC) analysis for data showed that at a cutoff point of 1.62, neutrophil/lymphocyte percentage could predict asthma with a sensitivity of 66.7%, specificity of 75.6%, positive predictive value of 73.2%, negative predictive value of 69.4%, and accuracy of 71.1% (Table 2 and Fig. 1).

Neutrophil/lymphocyte percentage was higher in asthmatics with ACT less than 20 than those with ACT of at least 20, with statistically significant difference, whereas this percentage did not differ significantly with sex, age, or smoking (*P*>0.05; Table 3).

Data of the present study revealed that neutrophil/lymphocyte percentage was significantly and directly correlated with CRP and ACT (*r*=0.51, *P*=0.001 and *r*=0.33, *P*=0.028, respectively), whereas correlations between neutrophil/lymphocyte percentage and age,

Table 1 Age, sex, neutrophil/lymphocyte ratio, and C-reactive protein between patients and controls

	Case group (45)	Control group (45)	Test	*P* value
Sex				
Male	20 (44.4)	16 (35.6)	χ^2=0.74	0.39
Female	25 (55.6)	29 (64.4)		
Age (mean±SD) (years)	37.82±14.54	33.07±10.89	*t*=1.76	0.083
N/L ratio (mean±SD)	2.77±1.87	1.40±0.52	*t*=4.73	0.001**
CRP (mean±SD) (mg/l)	21.66±17.09	6.05±3.78	*t*=5.99	0.001**

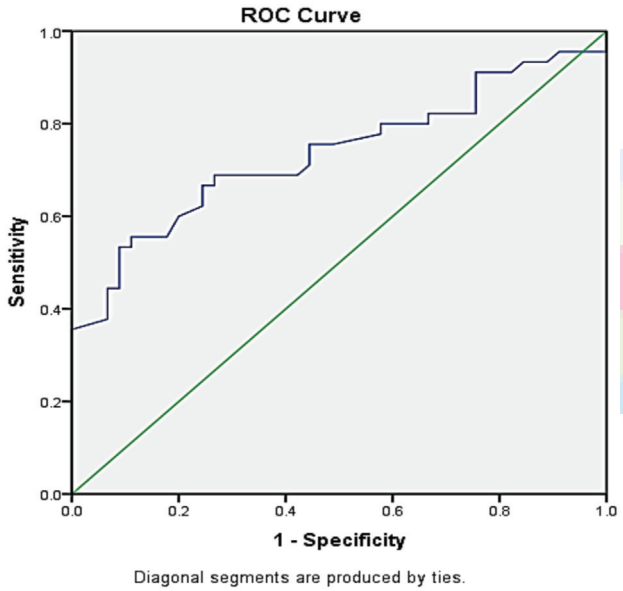
CRP, C-reactive protein; N/L, neutrophil/lymphocyte. **P<0.001, significant.

Table 2 Validity of neutrophil/lymphocyte as a predictor of disease

N/L	Case group (45)	Control group (45)	χ^2	*P* value
≥1.62	30 (66.7)	11 (24.4)	16.17	0.001**
<1.62	15 (33.3)	34 (75.6)		
AUC		0.735		
P value	0.001**			
95% CI	0.63–0.84			
Cutoff point		1.62		
Sensitivity		66.7		
Specificity		75.6		
PPV		73.2		
NPV		69.4		
Accuracy		71.1		

AUC, area under the curve; CI, confidence interval; N/L, neutrophil/lymphocyte; NPV, negative predictive value; PPV, positive predictive value. **$P<0.001$, significant.

Figure 1



ROC curve of neutrophil/lymphocyte as a predictor of disease.

eosinophils, IgE, Forced expiratory volume in first second (FEV_1%), duration of the disease, and number of attacks per year had no statistically significant difference (Table 4).

As seen in Table 5, CRP levels were higher in asthmatics with ACT less than 20 than those with ACT of at least 20, with statistically significant difference (P=0.005).

ROC analysis of cases with ACT of at least 20 versus those with ACT less than 20 revealed that at a cutoff point of 1.73, neutrophil/lymphocyte percentage could predict cases with low ACT with 72% sensitivity, 55% specificity, 66.7 positive predictive

Table 3 Neutrophil/lymphocyte ratio differences according to sex and smoking status

N/L	Mean±SD	Test	*P* value
Sex			
Males (20)	3.25±2.06	*t*=1.56	0.13
Females (25)	2.38±1.64		
Smoking			
Yes (13)	3.29±1.84	*t*=1.21	0.23
No (32)	2.55±1.87		
ACT			
>20 (20)	2.09±1.53	*t*=2.28	0.028*
<20 (25)	3.31±1.97		

ACT, asthma control test; N/L, neutrophil/lymphocyte. *$P<0.05$, significant.

Table 4 Correlations between neutrophil/lymphocyte ratio and age, eosinophils, C-reactive protein, ESR, IgE, FEV_1, asthma control test, duration of disease, and number of attacks per year

N/L	*r*	*P* value
Age (years)	–0.086	0.57
Eosinophil's ($\times10^9$/l)	–0.093	0.54
CRP (mg/l)	0.51	0.001*
ESR (mm/h)	0.043	0.78
IgE (UI/ml)	–0.18	0.24
FEV_1%	–0.26	0.08
ACT	0.33	0.28*
Duration (years)	–0.258	0.058
Number of attacks per year	–0.221	0.145

ACT, asthma control test; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; FEV_1, Forced expiratory volume in first second; N/L, neutrophil/lymphocyte. *Significant.

Table 5 Comparison of C-reactive protein between patients with asthma control test above and below 20

CRP	Mean±SD	Test	*P* value
ACT			
>20 (20)	13.95±6.37	*t*=2.93	0.005*
<20 (25)	27.83±20.35		

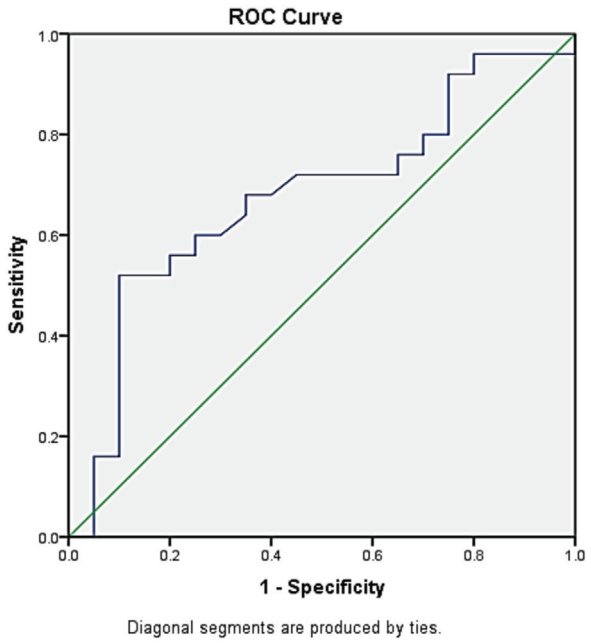
ACT, asthma control test; CRP, C-reactive protein. *Significant.

Table 6 Validity of neutrophil/lymphocyte as a predictor of low asthma control test among case group

N/L	ACT		χ^2	*P* value
	<20 (25)	≥20 (20)		
≥1.73	18 (72.0)	9 (45.0)	3.38	0.066
<1.73	7 (28.0)	11 (55.0)		
AUC		0.68		
P value		0.042*		
95% CI		0.52–0.84		
Cutoff point		1.73		
Sensitivity		72.0		
Specificity		55.0		
PPV		66.7		
NPV		61.1		
Accuracy		64.4		

ACT, asthma control test; CI, confidence interval; N/L, neutrophil/lymphocyte; NPV, negative predictive value; PPV, positive predictive value. *significant.

Figure 2



ROC curve of neutrophil/lymphocyte as a predictor of low asthma control test.

Table 7 Comparison between controlled and uncontrolled cases regarding TLC, duration/year, onset of the disease, and number of attacks per year)

	ACT≥20 (20) (mean ±SD)	ACT<20 (25) (mean ±SD)	Control group (45) (mean ±SD)	Statistical test	*P* value
TLC	6.24 ±1.08	6.52 ±1.44	6.11±0.75	*F*=1.09	0.34
Duration (/year)	4.30 ±1.52	5.27 ±1.94	–	Student *t*=1.88	0.07
Onset by age	27.84 ±4.78	30.0 ±4.84	–	Student *t*=1.50	0.14
Number of attacks/ years	2.23 ±1.11	3.15 ±1.76	–	Student *t*=2.15	0.038*

ACT, asthma control test; TLC, total leukocyte count. *significant.

value, 61.1 negative predictive value, and 64.4 accuracy (Table 6 and Fig. 2).

No statistically significant difference was found between patients with (ACT<20) and those with (ACT≥20) as regards TLC, onset and duration of the disease, while there was significant difference between them as regard number of attacks per year (ACT<20, 3.15±1.76 and ACT≥20, 2.23±1.11; Table 7).

Discussion

Neutrophil/lymphocyte percentage is an important marker of inflammation that can be obtained by division of absolute neutrophil count by absolute lymphocyte count. This study assessed the significance of neutrophil/lymphocyte percentage in asthmatics and its correlation with ACT plus other parameters in asthma. In the present study, the number of controlled and partially controlled cases (ACT≥20) was 20 (44.4%) and uncontrolled cases was 25 (55.5%). Gungen and Aydemir [8] found that controlled and partially controlled cases represented 51.4% and uncontrolled ones represented 48.95%. A multicenter study of 10 large developed cities in China has reported that 28.7 and 45% of asthmatic patients achieved full and partial control, respectively, according to GINA [9]. In a study done by Yan *et al.* [10] based on ACT sores, they found good asthma control in 31.61% of patients with moderate or severe asthma, partial asthma control in 40.27%, and poor asthma control in 28.12%. Price *et al.* [11] found that asthma was uncontrolled in 76% of the participants. Zhong *et al.* [12] found that asthma was controlled in 44.9% and uncontrolled in 55.1% of the study patients. They found that high rate of uncontrolled asthma was found in patients with treatment nonadherence, poor adherence, and nonschooling. In PRIMA study done by Allegra *et al.* [13], 64.4% of the patients had controlled asthma, 15.8% partly controlled, and 19.8% were uncontrolled. The current study indicated that neutrophil/lymphocyte percentage was higher in asthmatics than controls (with statistically significant value). It is directly correlated with CRP and ACT. These results were in agreement with those of Gungen and Aydemir [8] who found neutrophil/lymphocyte percentage to be higher in asthmatics versus control group (with statistically significant value) and to be inversely related to asthma control status.

Moreover, in agreement with this work results, Dogru and Mutlu [14] in children found neutrophil/lymphocyte percentage to be higher in asthmatics than the healthy control group. They suggested that neutrophil/lymphocyte percentage could be used to detect systemic inflammation in asthmatic children.

On the contrary, and in disagreement with the current work, Imtiaz *et al.* [15] did not find significant correlation between neutrophil/lymphocyte percentage with asthma control, but identification of asthma in this study was ensured by personal reporting, and neutrophil/lymphocyte percentage was not compared with controls.

In the present study, mean neutrophil/lymphocyte percentage was higher in asthmatics with ACT less than 20 versus those having ACT at least 20 (with

statistically significant difference), which means that neutrophil/lymphocyte percentage increases as asthma becomes uncontrolled. Gungen and Aydemir [8] showed that as asthma becomes uncontrolled, neutrophil/lymphocyte percentage is increased.

The present study showed that a cutoff point of 1.62, neutrophil/lymphocyte percentage could detect asthma with a sensitivity of 66.7% and specificity of 75.6% (area under the curve (AUC)=0.735, *P*=0.001), and at a cutoff point of 1.73, neutrophil/lymphocyte percentage could detect uncontrolled asthma (low ACT<20) with a sensitivity of 72% and a specificity of 55% (AUC=0.68, *P*=0.042). Zhang *et al.* [16] identified reduced blood lymphocytes and elevated neutrophil/lymphocyte ratio (NLR) in neutrophilic asthma, which may reflect systemic inflammation and could help in detecting uncontrolled asthma. They found that neutrophil to lymphocyte ratio cutoff point of 1.74 could detect neutrophilic asthma with sensitivity 76.9% and specificity of 41.6 (AUC=0.612, *P*=0.035) for. Lee *et al.* [17] found that NLR of 2.8 was considered an optimal cutoff value with maximal sensitivity and specificity for respiratory hospitalization in chronic obstructive pulmonary disease (COPD) patients; following ROC curve analysis, the sensitivity and specificity were 60.0 and 60.9%, respectively. Shi *et al.* [18] found that optimal cutoff value of NLR was 2.58 for diagnosis of acute exacerbations of bronchial asthma with sensitivity of 82.8% and specificity of 81.1%, and they concluded that peripheral blood NLR was increased in asthmatic patients. Jiang *et al.* [19] found that NLR with a cutoff value of 0.98 was able to discriminate children with recurrent wheezing, and it could be used as a potent diagnostic index for pediatric with recurrent wheeze.

The current work found that neutrophil/lymphocyte percentage was directly proportional to serum CRP levels. This finding was also obtained by Gunay *et al.* [20] who studied 269 patients with COPD and found directly proportional relation between neutrophil/lymphocyte percentage and CRP. This correlation is consistent with the fact that CRP is an acute-phase reactant synthesized by hepatocytes in response to inflammation [21] and neutrophil/lymphocyte percentage reflects the relationship of lymphomononuclear with neutrophilic arms of the process. This is considered as an evidence of the overall inflammatory status of the body [22].

The present study found that CRP was higher in asthmatics versus control group, and poorly controlled asthmatics (with ACT<20) had higher CRP levels than those with a better control (ACT≥20) (both have statistically significant difference). Similar results were shown by Hoshino *et al.* [23] who found significantly higher CRP concentrations in asthmatic patients than controls and a positive correlation between CRP and asthma severity. In contrast, Sigari and Ghasri [24] found no correlation between degree of systemic inflammation estimated by CRP and ACT.

The current study found neutrophil/lymphocyte percentage did not differ significantly regarding sex, age, or smoking among asthmatics; in other words, NLR was not substantially affected by these parameters. This result agreed with that of Dogru and Mutlu [14] who found a nonsignificant difference in neutrophil/lymphocyte percentage between studied groups regarding sex and smoking. They also found a nonsignificant relation between neutrophil/lymphocyte percentage and FEV_1. Gungen and Aydemir [8] also disclosed nonsignificant correlation between NLR and pulmonary functions, which was also in agreement with our result.

The current study found that neutrophil/lymphocyte percentage had a nonsignificant negative correlation with eosinophils and IgE, duration of the disease, and number of attacks per year, which agreed with Gungen and Aydemir [8] who showed that neutrophil/lymphocyte percentage did not have a relation with IgE, duration of the disease, and number of attacks per year. Moreover, our study did not find a significant difference in total leukocyte count (TLC) and onset and duration of disease between controlled asthmatic cases (ACT≥20) and uncontrolled patients (ACT<20), whereas the difference between controlled and controlled groups was statistically significant regarding the number of attacks per year, which was higher in uncontrolled group (3.15±1.76) versus controlled one (2.23±1.11). Yildiz [25] found that the number of patients requiring hospitalizations or unscheduled visits was lower in controlled (1.8 and 1.6%) than partly controlled (5.1 and 11.5%) and uncontrolled (6.4 and 18.6%) cases.There are some limitations in this study: the first was the relatively small size number of included subjects, and second, we did not set a specific blood sampling time although circadian variations in circulating neutrophil and lymphocyte counts were reported. The strengths of our study included patients were accurately diagnosed with asthma according to clinical data and spirometry, and no coexistent chronic diseases and infections were

present, which could affect neutrophil to lymphocyte percentage.

Conclusion

The present work demonstrated that the neutrophil/lymphocyte percentage was elevated in asthmatics especially uncontrolled and that this percentage could predict uncontrolled asthma with high sensitivity and specificity. Many advantages of neutrophil/lymphocyte percentage (quick, cheap, and easily measured in routine CBC test) make it a possible useful bedside test for asthma control.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Global Initiative for Asthma. Global strategy for asthma management and prevention. GINA 2018; 2:28.

2 Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, *et al.* Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL study. Am J Respir Crit Care Med 2004; 170:836–844.

3 Sekerel BE, Soyer OU, Keskin O, Uzuner N, Yazicioglu M, Kiliç M, *et al.* The reliability and validity of Turkish version of Childhood Asthma Control Test. Qual Life Res 2012; 21:685–690.

4 Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, *et al.* Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol 2004; 113:59–65.

5 Fu JJ, McDonald VM, Gibson PG, Simpson JL. Systemic inflammation in older adults with asthma-COPD overlap syndrome. Allergy Asthma Immunol Res 2014; 6:316–324.

6 6.England JM, Rowan RM, van Assendelft OW, Coulter WH, Groner W, Jones AR, *et al.* Protocol for evaluation of automated blood cell counters. International Committee for Standardization in Haematology (ICSH). Clin Lab Haematol 1984; 6:69–84.

7 Westergren A. Studies of suspension stability of the blood in pulmonary tuberculosis. Am Rev Tuberc 1921; 14:94–97.

8 Gungen AC, Aydemir Y. The correlation between asthma disease and neutrophil to lymphocyte ratio. Res J Allergy Immunol 2017; 1:1.

9 Su N, Lin J, Chen P, Li J, Wu C, Yin K, *et al.* Evaluation of asthma control and patient's perception of asthma: findings and analysis of a nationwide questionnaire-based survey in China. J Asthma 2013; 50:861–870.

10 Yan BD, Meng SS, Ren J, Lv Z, Zhang QH, Yu JY, *et al.* Asthma control and severe exacerbations in patients with moderate or severe asthma in Jilin Province, China: a multicenter cross-sectional survey. BMC Pulm Med 2016; 16:130.

11 Price D, Dale P, Elder F, Elder F, Champank R. Types, frequency and impact of asthma triggers on patients 'lives: a quantitative study in five European countries. J Asthma 2014; 51:127–135.

12 Zhong N, Lin J, Zheng J, *et al.* Uncontrolled asthma and its risk factors in adults chineses asthmatic patients. Ther Adv Respir Dis 2016; 10:507–517.

13 Allegra L, Cremonesia G, Girbino G, Ingrassia E, Marsico S, Nicolini G, *et al.* Real-life prospective study on asthma control in Italy: cross-sectional phase results. Respir Med 2012; 106:205–214.

14 Dogru M, Yesiltepe Mutlu RG. The evaluation of neutrophil-lymphocyte ratio in children with asthma. Allergol Immunopathol (Madr) 2016; 44:292–296. ?

15 Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, Rao S. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med 2012; 5:2.

16 Zhang XY, Simpson JL, Powell H, Yang IA, Upham JW, Reynolds PN, *et al.* Full blood count parameters for the detection of asthma inflammatory phenotypes. Clin Exp Allergy 2014; 44:1137–1145.

17 Lee SJ, Lee HR, Lee TW, Lim S, Go SI, *et al.* Usefulness of neutrophil to lymphocyte ratio in patients with chronic obstructive pulmonary disease: a prospective observational study. Korean J Intern Med 2016; 31:891–898.

18 Shi G, Zhao JW, Ming L. Clinical significance of peripheral blood neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in patients with asthma. Nan Fang Yi Ke Da Xue Xue Bao 2017; 37:84–88.

19 Jiang C, Yu H, Zhu W, Xu J, Lou B, Sun Q, *et al.* Neutrophil lymphocyte ratio in children with recurrent wheeze. Pediatr Allergy Immunol Pulmonol 2017; 30:4.

20 Gunay E, Sarinc, Ulasli S, *et al.* Neutrophil to lymphocyte ratio in chronic obstructive pulmonary disease: a retrospective study inflammation. Inflammation; 37:374–380.

21 Castell JV, Gómez-Lechón MJ, David M, Fabra R, Trullenque R, Heinrich PC. Acute-phase response of human hepatocytes: regulation of acute-phase protein synthesis by interleukin-6. Hepatology 1990; 12:1179–1186.

22 Biyik M, Ucar R, Solak Y, Gungor G, Polat I, Gaipov A, *et al.* Blood neutrophil-to-lymphocyte ratio independently predicts survival in patients with liver cirrhosis. Eur J Gastroenterol Hepatol 2013; 25:435–441.

23 Hoshino M, Ohtawa J, Akitsu K. Increased C-reactive protein is associated with airway wall thickness in steroid-naive asthma. Ann Allergy Asthma Immunol 2014; 113:37–41.

24 Sigari N, Ghasri H. Correlation between hs-CRP and asthma control indices. Tanaffos 2013; 12:44–48.

25 Yildiz F. ASIT Study Group. Factors influencing asthma control: results of a real life prospective zobservational asthma inhaler treatment (ASIT). J Asthma Allergy 2013; 6:93–101.