



Diagnostic Value of Neutrophil-Lymphocyte Ratio in Diagnosis of Asthma: A Case-Control Study in Baghdad

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ARTICLE INFO

Article history:

Received 10 July 2019

Revised 21 August 2020

Accepted 28 September 2020

Published online 03 October 2020

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ABSTRACT

Bronchial asthma is a chronic inflammatory illness of the airways accompanied by systemic inflammation in almost all affected patients. This study aimed to evaluate the diagnostic value of neutrophil-lymphocyte ratio (NLR) in the detection of asthma cases in Baghdad, Iraq. It was a case-control study that included a total of 62 adult patients with asthma who were clinically diagnosed by a consultative physician, and 68 age- and gender-matched apparently healthy subjects as a control group. Samples of peripheral blood were collected from each participant. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The receiver operating characteristic (ROC) curve was used to assess the diagnostic value of NLR in the detection of asthma cases. Mean NLR in asthma patients was 2.33 ± 0.89 compared with 1.82 ± 1.04 in controls with a highly significant difference. The area under the curve (AUC) was 0.886 (95% CI = 0.762-0.951), $p = 0.002$. The sensitivity and specificity of the test at NLR = 2.11 were 82.8% and 73%, respectively. There was a significant positive correlation between NLR and the number of asthma attacks/year ($r = 0.247$, $p = 0.037$). Thus, NLR is a reasonable, easy-to-use, and cheap test that can be routinely used to evaluate the inflammatory response in asthmatic patients.

Keywords: Asthma, neutrophil-lymphocyte ratio, receiver operating characteristic curve, inflammation.

Introduction

Bronchial asthma is a chronic inflammatory illness of the airways affecting 1-18% of the population in different countries.¹ The persistence and relapse of asthma are the main causes of the long-term suffering in affected patients. Pathologically, asthma is characterized by numerous inflammatory cells and mediators. Although the physiological effects of such inflammation are most significant on medium-sized bronchi,² in particular, systemic inflammation does present in almost all asthma patients. The common feature of this inflammation is reflected by increasing the serum level of pro-inflammatory cytokines such as interleukin (IL)-6 and tumour necrosis factor- α (TNF- α).³ This trend of asthma course alerts the researchers to investigate the role of inflammatory markers in the diagnosis of occurrence and severity of asthma. Recently, some of these markers, such as exhaled nitric oxide,⁴ urine eosinophil X protein,⁵ peripheral blood matrix metalloproteinase-9 (MMP-9)⁶ and many others have been investigated with different degrees of validity. However, most of these markers have some drawbacks such as high cost and inconvenience. Neutrophil-lymphocyte ratio (NLR) could be an essential indicator for systemic inflammation as its components are part of a routine investigation, inexpensive and could be calculated effortlessly.⁷ During the last few years, NLR has been shown to indicate the degree

of body inflammation in a variety of inflammatory illnesses and are associated with the stage and grade of a particular illness.^{8,9} The present study aimed to assess the diagnostic value of NLR in the detection of asthma in adult patients in Baghdad, Iraq.

Materials and Methods

Sample collection

This is a case-control study which included a total of 62 adult patients (age 18-63 years, 36 males and 26 females) with asthma who were attending Al-Zahra's Consultative Center for Allergy and Consultative Clinic for Asthma, Baghdad during the period from February to August 2019. Diagnosis of asthma was primarily grounded on medical history, clinical features and physical examination, while the final diagnosis was performed according to the criteria of Global Initiative for Asthma.¹⁰ Patients with exacerbation, having systemic steroids therapy within the last month prior to sampling, and those with any other systemic disease such as cardiovascular, hepatic, or renal diseases, diabetes mellitus (DM), neoplasms, and any systemic inflammatory disorder were excluded from the study. Other 68 apparently healthy subjects (age 19-68 years, 41 males and 27 females) were recruited to represent the control group. Current or ex-smokers were excluded from patients or controls. This study was approved by the review board of Technical Institute, Al-Dewaniya (No. 2018/96).

Laboratory investigations

Three mL of fasting peripheral blood was collected from each participant. Hematology auto-analyzer (Huroba ABX, India) was used to measure blood parameters. The calculation of NLR was performed according to the following formula: Absolute neutrophil count/absolute lymphocyte. Written consent from each participant was obtained prior to sample collection after explaining the aim of the study. Each patient had the complete unconditioned choice to

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Citation: Chalooob FA, Al-Mayah QS, Jawed TI. Diagnostic Value of Neutrophil-Lymphocyte Ratio in Diagnosis of Asthma: A Case-Control Study in Baghdad. Trop J Nat Prod Res. 2020; 4(9):523-526. doi.org/10.26538/tjnpr/v4i9_5

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

withdraw at anytime. The confidentiality of data during the course of the study was definite and the patients were guaranteed that data will be used for research purposes only. Socio-demographic and clinical data including; age, sex, body mass index (BMI), duration of asthma, and number of attacks/year were collected through direct interviews or from patients' records.

Statistical analysis

All statistical tests were achieved with SPSS statistical software, version 24 (IBM Corporation, USA). Shapiro Wilk test was used to examine whether variables deviate from the normal distribution. Variables having normal distribution were expressed as mean (standard deviation). Categorical variables were presented as frequency and percentages. Independent student t-test was used to compare any two groups of continuous data, while Chi-square/Fisher's exact test was employed to find out the statistical significance between categorical variables, chi-square test was performed. Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic value of NLR in the detection of asthma. The correlation between NLR and each of disease duration and number of attacks was explored using Pearson's correlation. The significant level of statistics was set at $p < 0.05$.

Results and Discussion

Mean age of the patients and controls was 38.17 ± 11.7 years and 42.81 ± 10.4 years, respectively with no significant difference. Likewise, the two groups were comparable in terms of BMI, gender distribution Hb concentration, and total leukocyte count with no significant differences. However, asthma patients showed significantly higher absolute neutrophil count than controls ($4.61 \pm 1.4 \times 10^3/\text{mL}$ vs. $3.72 \pm 1.22 \times 10^3/\text{mL}$). Mean duration of asthma in the patients was 8.22 ± 6.91 years, while there were 2.7 ± 0.84 attacks/year. Finally, Mean NLR in asthma patients was 2.33 ± 0.89 compared with 1.82 ± 1.04 in controls with a highly significant difference (Table 1).

Diagnostic value of Neutrophil Lymphocyte ratio

The receiver operating characteristic (ROC) curve was used to assess the diagnostic value of NLR in the detection of asthma cases compared with healthy controls. The result is depicted in Figure 1. The area under the curve was 0.886 (95% CI = 0.762-0.951), $p = 0.002$. The sensitivity and specificity of the test at NLR = 2.11 were 82.8% and 73%, respectively. The test has a positive predictive (PPV) value of 75% and a negative predictive value of 81.5%.

In fact, this study confirmed the results of many previous studies in this regard. However, the present study investigated this marker among the Iraqi population. It is well known that different ethnicities

can vary in their response to various illnesses, and what can be verified as a marker in a specific population may not be suitable in another.

The current result also is in line with the study of Hendy *et al.*¹¹ who investigated the association of NLR with bronchial asthma in 45 Egyptian patients and 45 healthy subjects. At a cut off value of 1.62, the sensitivity and specificity of NLR in the diagnosis of asthma were 66.7% and 75.6%, respectively, while PPV and NPV were 73.2% and 71.1%, respectively. In a large Turkish study, Dogru *et al.*¹² calculated the NLR in 469 patients with asthma and 170 individuals free from allergic disease. Mean NLR was found to be 2.07 ± 1.41 and 1.77 ± 1.71 , respectively with a significant difference. Almost similar results were obtained in another Turkish study.¹³ Fu *et al.*³ evaluated systemic inflammation in 50 adult Australian patients with asthma. They found that the number of neutrophils in sputum was more in asthmatics compared to controls. Shi *et al.*¹⁴ found that the ideal cut off value of NLR was 2.58 for diagnosis of acute exacerbations of bronchial asthma with sensitivity and specificity of 82.8% and 81.1%, respectively. The authors concluded that peripheral blood NLR is raised in asthma patients. Jiang *et al.*¹⁵ reported a relatively low NLR cutoff value of 0.98 than can be used to discriminate children with recurrent wheezing and could be used as a potent diagnostic tool for pediatric with recurrent wheeze. Nevertheless, some studies have failed to find a significant association between NLR and asthma.¹⁶

Correlation of NLR with disease duration and numbers of attacks

As NLR showed a significant association with Asthma, Pearson's correlation test was used to explore the possible correlation of this marker with the duration of asthma and the number of an asthma attacks. There was a non-significant positive correlation between NLR and disease duration ($r = 0.169$, $p = 0.159$) as shown in Figure 2. On the other hand, there was a significant positive correlation between NLR and number of asthma attacks/year ($r = 0.247$, $p = 0.037$) (Figure 2).

Thus, NLR does not only detect asthma but also can indicate the severity of the disease. This is in accordance with the study of Mochimaru *et al.*¹⁷ who investigated the relationship between NLR the existence of a severe exacerbation prospectively in 104 Japanese patients. Interestingly, NLR was significantly correlated with severe exacerbation after one year of assessment. The ROC curve results demonstrated that the cutoff value of NLR for severe exacerbation was 2.1 (area under the curve 0.63, sensitivity 65%, and specificity 60%). Neutrophils are of particular importance in the immune system. These cells can modify the functions of epithelial cells, mast cells, and macrophages. Furthermore, they play a crucial role in the inflammatory response.¹⁸ Lymphocyte, on the other hand, are integral to the development of a complete innate and adaptive immune response. From the diagnostic point of view, leukocytes, in general, are the classic inflammatory markers that are easy to measure.¹⁹

Table1: Demographic and Clinical Characteristic of the Study Population

Characteristics	Patients (N = 62)	Controls (N = 68)	P-value
Age (years)	38.17 ± 11.7	42.81 ± 10.41	0.114
Range	18-63	19-68	
BMI (kg/m ²)	27.73 ± 4.34	28.12 ± 4.2	0.481
Gender			
Male	36(58.06%)	41(60.29%)	0.896
Female	26(41.94%)	27(39.71%)	
Hb (g/dL)	13.22 ± 2.92	13.28 ± 2.86	0.883
Total WBC ($\times 10^3/\text{mL}$)	8.81 ± 3.77	7.6 ± 2.65	0.208
Neutrophil ($\times 10^3/\text{mL}$)	4.61 ± 1.4	3.72 ± 1.22	0.011
Lymphocyte ($\times 10^3/\text{mL}$)	2.42 ± 0.81	2.11 ± 0.71	0.214
Duration of the disease (years)	8.22 ± 6.91	-	-
Number of attacks/year	2.7 ± 0.84	-	-
Neutrophil-lymphocyte ratio	2.33 ± 0.89	1.82 ± 1.04	0.012

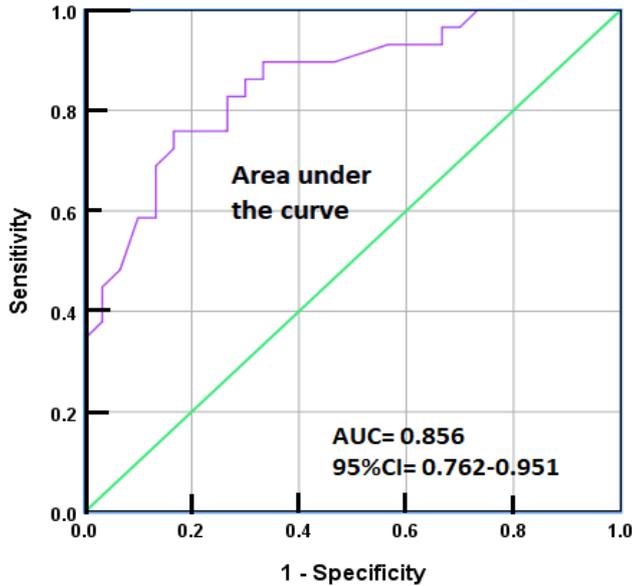


Figure 1: Receiver operating characteristic curve for NLR in the context of discrimination between asthma and control

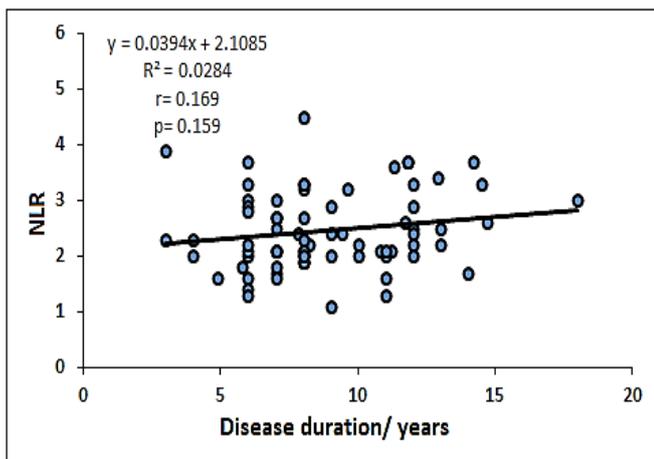


Figure 2: Correlation between NLR and the duration of asthma

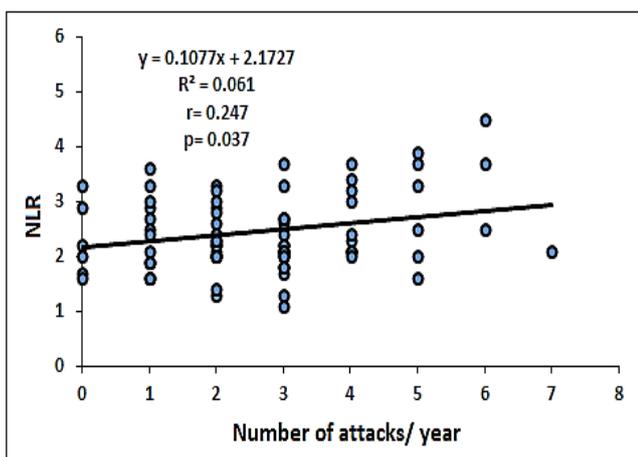


Figure 3: Correlation between NLR and asthma attacks/year

However, measuring the individual types of cells such as lymphocytes, neutrophils, monocytes or even the total leukocyte count cannot be associated with specific disease or condition. On the other hand, NLR comprises a combination of two markers and it is superior to the other leukocyte parameter due to the stability of the ratio compared with the absolute count that may be altered by various physiological conditions.²⁰

Conclusion

The present data indicate that NLR has good diagnostic value in the context of discrimination between asthmatic and non-asthmatic patients. This merit can be clinically exploited especially to differentiate asthmatic patients from other patients with inflammatory disorders. Therefore, the study recommends that NLR is a reasonable and easy-to-use marker for asthma as an evaluation.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

The authors highly appreciate the great help of all staff at Al Zahra's Consultative Center for Allergy, Baghdad during the blood sample collection. We are extremely grateful to all participants in control group, without whom the study could not be achieved.

References

1. Prakash AK, Datta B, Jaiswal A. Acute Exacerbation of Asthma and Chronic Obstructive Pulmonary Disease. In: Richhariya D, Fares S, Bajan K, Pawaiya S. (eds.). Textbook of Emergency and Trauma Care. Jaypee Brothers Medical Publishers, New Delhi, 2018. 228 p.
2. Ober C. Perspectives on The past decade of asthma genetics. *J Allerg Clin Immunol.* 2005; 116:274-278.
3. Fu JJ, McDonald VM, Gibson PG, Simpson JL. Systemic inflammation in older adults with asthma-COPD overlap syndrome. *Allerg Asthma Immunol Res.* 2014; 6:316-324.
4. Nuijsink M, Hop WC, Sterk PJ, Duiverman EJ, De Karrasch S, Linde K, Rücker G, Sommer H, Karsch-Völk M, Kleijnen J, Jörres RA, Schneider A. Accuracy of FENO for diagnosing asthma: a systematic review. *J Thorax.* 2016; 10:208704.
5. Jongste JC. Urinary eosinophil protein X in childhood asthma: relation with changes in disease control and eosinophilic airway inflammation. *Mediators Inflamm.* 2013; 2013:532619.
6. Grzela K, Litwiniuk M, Zagorska WA. Airway remodeling in chronic obstructive pulmonary disease and asthma: the role of matrix metalloproteinase-9. *Arch Immunol Ther Exp. (Warsz).* 2016; 64(1):47-55.
7. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, Lyisoy A. The relation between atherosclerosis and the neutrophil-lymphocyte ratio. *Clin Appl Thromb Hemost.* 2015; 22(5):405-411.
8. Wiwanitkit V. Neutrophil to lymphocyte ratio in allergic rhinitis. *Eur Arch Otorhinolaryngol,* 2016; 273(10):3443.

9. Lee H, Um SJ, Kim YS, Kim DG, Jang AS, Choi HS, Kim YH, Kim TE, Ha YK, Jung K. Association of the neutrophil-to lymphocyte ratio with lung function and exacerbations in patients with chronic obstructive pulmonary disease. *PLoS One* 2016; 11(6):e0156511.
10. Global Initiative for Asthma (GINA) [homepage on the Internet]. 2012. Available from: <http://www.ginasthma.org>. Accessed May 29, 2015.
11. Hendy RM, Elawady MA, Mansour AI. Assessment of neutrophil/lymphocyte percentage in bronchial asthma. *Egypt J Chest Dis Tuberc*. 2019; 68:74–79.
12. Dogru M, Yesiltepe Mutlu RG. The evaluation of neutrophil- lymphocyte ratio in children with asthma. *Allergol Immunopathol (Madr)*. 2016; 44(4):292-296.
13. Gungen AC and Aydemir Y. The correlation between asthma disease and neutrophil to lymphocyte ratio. *Res J Allergy Immunol*. 2017; 1(1):1-4.
14. Shi G, Zhao JW, Ming L. Clinical significance of peripheral blood neutrophillymphocyte ratio and platelet-lymphocyte ratio in patients with asthma. *Nan Fang Yi Ke Da Xue Xue Bao* 2017; 37:84–88.
15. Jiang C, Yu H, Zhu W, Xu J, Lou B, Sun Q, Yang X, Meng L, Lu S. Neutrophil lymphocyte ratio in children with recurrent wheeze. *Pediatr Allergy Immunol Pulmonol*. 2017; 30:4.
16. Sagmen SB and Kiral N. The evaluation of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in asthma control. *Revue Francaise D'allergologie* 2020; 60:20-23.
17. Mochimaru T, Ueda S, Suzuki Y, Asano K, Fukunaga K. Neutrophil-to-lymphocyte ratio as a novel independent predictor of severe exacerbation in patients with asthma. *Ann Allergy Asthma Immunol*. 2019; 122(3):337-339.
18. von Vietinghoff S and Ley K. Homeostatic regulation of blood neutrophil counts. *J Immunol*. 2008; 181(8):5183-5188.
19. Torun S, Tunc BD, Suvak B, Yildiz H, Tas A, Sayilir A, Ozdern YO, [Beyazit](#) Y, Kayacetin E. Assessment of neutrophil-lymphocyte ratio in ulcerative colitis: A promising marker in predicting disease severity. *Clin Res Hepatol Gastroenterol*. 2012; 36:491-497.
20. Nunez J, Nunez E, Bodi V, Sanchis J, Miñana G, Mainar L, Santas E, Merlos P, Rumiz E, Darmofal H, Heatta AM, Llàcer A. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in ST segment elevation myocardial infarction. *Am J Cardiol*. 2008; 101:747-752.