DOES NEUTROPHIL / LYMPHOCYTE RATIO CONTRIBUTE TO DIAGNOSTICS IN PATIENTS WITH FASCIOLIASIS?

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ABSTRACT

Introduction: Fasciolia sp. is a trematode causes infection by settling in the liver bile ducts of domestic animal and human liver. Fascioliasis is a parasite disease that might have changes in liver parenchyma and in bile ducts. Many inflammatory reactions occur during the settlement of larvae and mature parasites into the liver. The neutrophil/lymphocyte ratio (NLR) has become a prominent marker of underlying inflammation. The objective of the present study is to investigate the relationship between the hematological parameters in patients with fascioliasis.

Materials and methods: The diagnosis of fascioliasis was based on patient history, clinical and laboratory findings, radiological imaging (ultrasound), stool examination and IgG antibody titer determination by ELISA. Clinical and laboratory data were collected for 56 patients with fascioliasis, and diagnosed with serological and radiological imaging. 56 healthy volunteers were selected for the control group. Stool and blood samples were collected from patients with fascioliasis for serologic, biochemical, hematologic tests and ova examination. Total leukocyte, neutrophil, eosinophil and lymphocyte counts were recorded and NLR was calculated. ELISA antibody cut off titer value of patients with fascioliasis was 10> positive.

Results: We compared neutrophil/lymphocyte ratio, eosinophil/lymphocyte ratio, the relation of eosinophilia and IgG antibody titers between two groups (patient and control groups). There was no statistically significant difference between patients and healthy controls neither based on age and gender nor NLR. According to these findings, NLR can not be considered as a diagnostic marker in fascioliasis.

Conclusion: As a result, it was determined that NLR is not a crucial indicator of inflammation in parasitic fascioliasis. Extensive studies are need to be done to clarify the correlation between NLR and progression of other parasitic diseases.

Keywords: Fascioliasis, neutrophil/lymphocyte ratio, contribution to diagnosis.

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Introduction

Fasciola hepatica and F. gigantica, two trematode species of Fasciolidae family, settle in human liver bile ducts and cause fascioliasis. Humans might be infected by the ingestion of uncooked aquatic plants which possess cysted metacercariae or by drinking contaminated water[1,2]. The classical diagnosis of fascioliasis is conducted by determination of eggs in feces. When eggs are not observed in stool, serological and radiological methods which are more sensitive are used in the diagnosis of fascioliasis[1,3]. Fascioliasis is a disease that might have an acute or chronic prognosis due to the changes in liver parenchyma (young parasites) and in bile ducts (mature parasites) and characterized by different clinical findings varying from asymptomatic infection to severe hepatic cirrhosis.

Three most important signs of the disease are pain, fever and liver enlargement. Abdominal pain, fever, weight loss and fatigue are also common symptoms[4-7]. In laboratory findings, it has been observed that Eosinophilia, total IgE, AST, ALT, GGT levels rise in patients with fascioliasis[1,4,8]. The neutrophil/lymphocyte ratio (NLR) has become a prominent marker of the underlying inflammation. NLR has been determined in several diseases[9-11] but there are few studies conducted to determine the relation between NLR and progression of infectious diseases. Furthermore, there is no study scrutinizing the relationship between fascioliasis severity and NLR. The objective of the present study is to investigate the relationship between hematological parameters in patients with fascioliasis.

Materials and methods

Patients admitted to Dicle University, Faculty of Medicine, Gastroenterology and Infectious Diseases Department outpatient clinic in Diyarbakır are included prospectively in the present study. Fascioliasis diagnosis was based on patient history, clinic, laboratory findings, radiological imaging (ultrasound), stool examination and IgG antibody titer determined with ELISA. In ELISA, the photometrical readings were performed at 450nm (TECAN SUNRİSE micro ELISA). The excretory/secretory antigens were used for immunodiagnosis of fascioliasis in the kit (values greater than 11.0 DRG Units=DU/ml were interpreted as seropositive, cut-off value 10). Clinical and laboratory data were collected from 56 patients with fascioliasis, which were diagnosed with serological and radiological imaging. 56 healthy volunteer were selected as the control group. Stool and blood samples were collected from fascioliasis patients for serologic, biochemical and hematologic tests and ova examination. Total leukocyte count, neutrophil, eosinophil and lymphocyte counts were recorded and NLR was calculated. Complete blood count analyses were performed with Beckman Coulter LH- 750 Hematology Analyzer (Beckman Coulter, Inc., Fullerton, CA, USA). NLR values and relationship between ELISA titers and eosinophil counts and relationship between ELISA titers and lymphocyte count were compared for the patient and control groups. Neutrophil / Lymphocyte ratio, ELISA-Eosinophil rates and distributions were statistically analyzed with Shapiro Wilk and Kolmogorov-Smirnov tests both in patient and control groups. Since the ratios

for the patient and control groups were distributed normally with small deviations (P> 0,05), they were evaluated with the Student-t test.

Results

There was no statistically significant difference between patients and healthy controls neither based on age and gender nor NLR and eosinophil / lymphocyte ratio (P> 0.05). Moreover, no significant correlation was determined between the eosinophil counts and ELISA antibody titers in patients with fascioliasis. Since NLR values were not significantly different in patients compared to controls when Student-t test was performed (p = 0.806), NLR can not be considered as a diagnostic marker in fascioliasis. (Figure 1). Pearson correlation value between eosinophil counts and ELISA titers was r = 0.12 in patients with fascioliasis and there was no significant correlation between the two values (p = 0.380) (Figure 2).
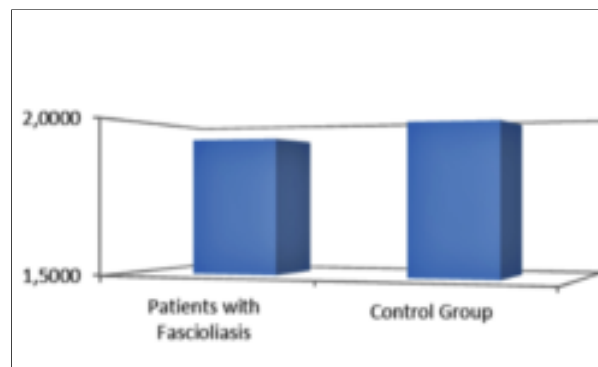

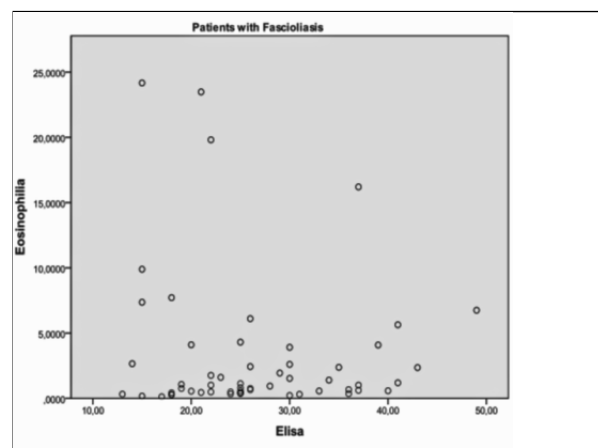**Figure 1**: Graph showing that the neutrophil lymphocyte ratio is not meaning.

Figure 2: Graphic showing that Pearson correlation value between Eosinophil and ELISA is not significant.

Discussion

There are several studies investigated NLR as a disease predictive marker. In these studies, the NLR values were determined in cardiovascular disease, chronic renal failure, malignancies, osteoporosis and Alzheimer's disease[12-15]. However, there are few studies which demonstrate the association between the severity of infectious diseases and NLR values. In particular, there is no study demonstrating the relation between NLR values and fascioliasis severity. Therefore, in our opinion present study has a significant value. In a study conducted by Marlies et al[16], the relationship between NLR value and malaria disease severity was investigated and a correlation of parasitemia and NLR value was observed. However, the difference was not statistically significant when compared to the control group. As a result, it was concluded that there is no marker available to demonstrate disease severity[16]. Our study fortifies those findings since there is no significant difference between fascioliasis patients and the control group based on NLR values.

On the other hand, in a study[17] on tuberculosis by Abakay et al, it was reported that NLR values were significantly higher in patients diagnosed with pulmonary tuberculosis when compared to the control group, and that NLR was an important marker of inflammation that could assist clinical determination of the severity of the disease[17]. Olt et al[18] also evaluated the efficacy of NLR in patients diagnosed with brucellosis and reported a significant association between NLR values in patient group with brucellosis when compared to the healthy control group. Furthermore, in another study investigating the relationship between NLR values and hepatitis C severity, it was found that the NLR values in chronic hepatitis C (CHC) patients were significantly higher than the healthy group. In the study, the researchers separated the CHC group into two subgroups as a group with advanced fibrosis (F3-4), and a group without advanced fibrosis (F1-2) and the highest NLR values were observed in advanced fibrosis group and they concluded that the NLR values could be a novel noninvasive marker for the prognosis of the CHC[19]. Moreover, in another study evaluating NLR values in patients with bloodstream infection, NLR was shown to be an independent risk factor for mortality[20].

As a result, although significantly higher NLR values were observed when compared to the healthy control group, in studies conducted to define the rela-

tion between NLR values and progression of bacterial and viral infections, there is no significant difference found in parasite infections including our study when patient NLR values were compared to the healthy volunteers. Based on our findings, it is suggested that the NLR values cannot be considered as a diagnostic and prognostic marker in fascioliasis.

In fascioliasis, eosinophilia is an important marker that facilitates the diagnosis of the disease[1, 8]. In this study when we compared ELISA antibody titers and eosinophil counts in patients, it was observed that there is no correlation between eosinophil counts and IgG antibody titers since several factors could raise the antibody titers such as the parasite load of the individual. As a result, comprehensive studies need to be done to determine the correlations between different parameters.

Finally, the NLR value is an important indicator of inflammation in microbial infections while this is not the case in parasitic diseases. In Fasciola hepatica infection, the NLR values do not show any correlation neither. Extensive studies need to be done to clarify the correlation between the NLR values and parasitic disease severity other than malaria and fascioliasis.

References

1) Mas-Coma S, Bargues MD, Valero MA. Fascioliasis and other plant-borne trematode zoonoses. Int J Parasitol 2005; 35: 1255-1278.

2) Maguire, J.H. Trematodes (Schistosomiasis) and other flukes. In: Mandell GL, Bennett JE, Dolin R. (Eds.). Principles and Practice of Infectious Diseases. New York, Churchill Livingstone. 2005; 3276-3285.

3) Dusak A, Onur MR, Cicek M, Firat U, Ren T, Dogra VS. Radiological Imaging Features of Fasciola hepatica Infection-A Pictorial Review. J Clin Imaging Sci 2012; 2: 1-8.

4) Garcia LS Diagnostic Medical Parasitology. Fifth Edition, ASM press, American Society for Microbiology. 2007; 432-436.

5) Berasain P, Carmona C, Frangione B, Dalton JP, Goni F. Fasciola hepatica: Parasite- Secreted Proteinases Degrade All Human IgG Subclasses: Determination of the Spesific Cleavage Sites and Identification of the Immunoglobulin Fragments Produced. Exp Parasitol 2000; 94: 99-110.

6) Marcos L, Maco V, Samalvides F, Terashima A, Espinoza JR, Gotuzzo E. Risk factors for Fasciola hepatica infection in children: a case-control study. Trans R Soc Trop Med Hyg 2006; 100: 158-166.

7) Markell EK, Voge M, John DT. Medical Parasitology.

Seventh Edition. Philadelphia :WB Saunders Co. 1992.

8) Karahocagil MK, Akdeniz H, Sunnetcioglu M, Cicek M, Mete R, et al. A familial outbreak of fascioliasis in Eastern Anatolia: a report with review of literature. Acta Trop 2011; 118: 177-183.

9) Templeton AJ, McNamara MG, ˇSeruga B, Vera-Badillo FE, Aneja P, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst 2014; 106: 124-130.

10) Nakano K, Hosoda M, Yamamoto M, Yamashita H. Prognostic significance of pre-treatment neutrophil: lymphocyte ratio in Japanese patients with breast cancer. Anticancer Res 2014; 34: 3819–3824.

11) Graziosi L, Marino E, Angelis V, Rebonato A, Cavazzoni E, Donini A. Prognostic value of preoperative neutrophils to lymphocytes ratio in patients resected for gastric cancer. Am J Surg 2014; 209: 333-337.

12) Sarraf KM, Belcher E, Raevsky E, Nicholson AG, Goldstraw P, Lim E. Neutrophil/lymphocyte ratio and its association with survival after complete resection in non-small cell lung cancer. J Thorac Cardiovasc Surg 2009; 137: 425-428.

13) Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 2006; 97: 993-996.

14) Ahsen A, Ulu MS, Yuksel S, Demir K, Uysal M, et al. As a new inflammatory marker for familial Mediterranean fever: Neutrophil-to-lymphocyte ratio. Inflammation 2013; 36:1357-1362.

15) Turkmen K, Erdur FM, Ozcicek F, Ozcicek A, Akbas EM, et al. Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients. Hemodial Int 2013; 17: 391-396.

16) Wolfswinkel ME, Vliegenthart-Jongbloed K, Mendonça Melo M, Wever PC, McCall MB, et al. Predictivevalue of lymphocytopenia and the neutrophil-lymphocyte count ratio for severe imported malaria. Malar J 2013; 12:101-109.

17) Abakay O, Abakay A, Sen HS, Tanrikulu CA. The Relationship Between Inflammatory Marker Level sand Pulmonary Tuberculosis Severity. Inflammation 2015; 38: 691-696

18. Olt S, Ergenç H, Açikgöz SB. Predictive Contribution of Neutrophil/Lymphocyte Ratio in Diagnosis of Brucellosis. Biomed Res Int 2015; 2015: 210502.

19) Abdel-Razik A, Mousa N, Besheer TA, Eissa M, Elhelaly R, et al. Neutrophil to lymphocyte ratio as a reliable marker to predict insulin resistance and fibrosis stage in chronic hepatitis C virus infection. Acta Gastroenterol Belg 2015; 78: 386-392.

20) Yang M, Li L, Su N, Lin J, Wang J. Dynamic monitoring of the neutrophil/lymphocyte ratio could predict the prognosis of patients with blood stream infection. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2015; 27: 471-476.

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