

# Correlation Between Liver Fibrous Level and Neutrophil Lymphocytes in Chronic Hepatitis B

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## ABSTRACT

**Objective:** Liver biopsy is the gold standard procedure to identify necro-inflammatory activity and fibrous grade in chronic liver disease. Recently, there has been increased interest in non-invasive tests to predict the degree of fibrosis hence, serum neutrophil lymphocyte ratio (NLR), has been utilized to elaborate systemic inflammation in various studies. In this study, we investigated the correlation between histopathologically liver fibrosis grade and serum NLR.

**Materials & Method:** Histopathological results of liver biopsy and neutrophil, lymphocyte values in complete blood count of 114 chronic hepatitis B patients who did not receive treatment were evaluated. The patients were divided into 3 groups: 21 patients with pathologically mild fibrosis (f 1 - 2) as group 1, 75 patients with moderate fibrosis (f 3 - 4) as group 2, and 18 patients with severe fibrosis (f 5 - 6) as group 3. NLR, mean values of the groups, sensitivity, specificity, positive and negative predictive values were calculated.

**Results:** There was no statistically significant difference between patient groups in terms of age and gender. When the groups were compared the sensitivity and specificity of NLR were low, and positive or negative predictive values were not significant.

**Conclusion:** Regarding the results of this study one can say that no correlation was found between NLR and liver fibrosis grade.

**Keywords:** NLR; Neutrophil Lymphocyte Ratio; Liver Fibrosis Grade; Sensitivity; Specificity

## Introduction

In chronic hepatitis B disease, defining the degree of liver fibrosis and chronic inflammatory activity has an important aspect in the treatment. It is known that lympho-mononuclear cells play a major role in the process of liver fibrosis. The gold standard examination in demonstrating inflammatory activity and the degree of fibrosis is liver biopsy [1]. Since every region of the liver is not affected in the same way in chronic hepatitis B disease, it is thought that a single biopsy sample does not always accurately reflect the characteristics of the disease and the degree of fibrosis. Modified Knodall classification is most commonly used in the histopathological examination of the liver. There is approximately 0.3 - 0.6% morbidity and 0.05% mortality risk in liver biopsy, and the obtained material should contain at least 2 cm and 11 - 15 portal areas [2,3]. For these reasons, various

studies on non-invasive tests have been carried out in recent years to predict the degree of liver fibrosis. The neutrophil lymphocyte ratio (NLR), which can be calculated in a complete blood count, is accepted as an indicator of subclinical inflammation [4]. NLR values are simple to calculate and are considerably cost-effective. In this study, we aimed to investigate the correlation between histopathologically liver fibrous grade and NLR.

## Materials & Method

The data of a total of 114 chronic hepatitis B patients, who were followed up in the hepatology outpatient clinic were retrospectively analyzed. Individuals had HBV DNA  $\geq 2000$  u/ml, underwent percutaneous liver biopsy and did not have any comorbid disease. NLR was calculated prior to liver biopsy. The degree of fibrosis was determined

by using the Modified Knodall classification in the pathology report of the patients included in the study, and they were divided into 3 groups as: group 1 mildly fibrous (f 1 – 2) with 21 patients, group 2 75 patients with moderate fibrosis (f 3 – 4) and group 3 18 patients with advanced fibrosis (f 5 – 6) (Table 1).

**Table 1:** Demographic characteristics of patient groups.

Groups	NLR	Age	
Group: 1, F:1 - 2 n: 21	1.4 ± 0.4	42.0±12	Male: 10 Female: 11
Group: 2 F:3 - 4 n: 75	1.8 ±0.9	46.67 ±12.0	Male: 40 Female: 35
Group: 3, F:5- 6 n: 18	2.1±1.0	43.40±17.0	Male: 8 Female: 10
Total, n:114	1.8 ± 0.8	44.3 ±13.8	

### Statistical Analysis

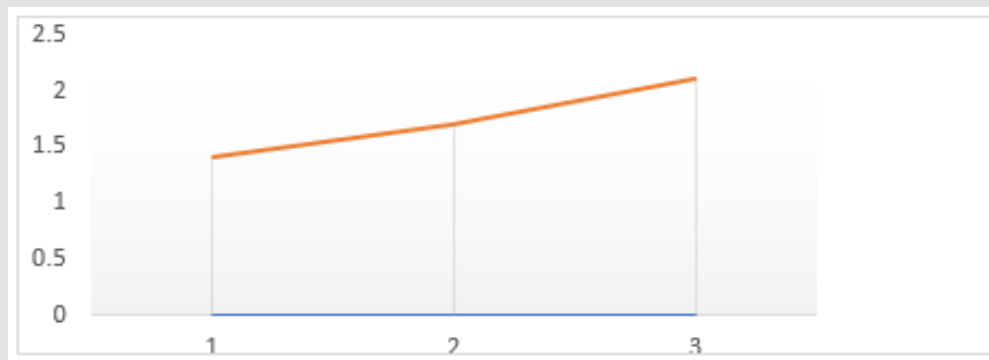
The progression in the fibrous degree of the groups and their NLR were statistically compared using the Mann-Whitney U test. Sensitivity, specificity, positive and negative predictive values for demonstrating fibrosis were calculated with 95% confidence intervals. SPSS 18.0 was used as a statistical package program for data analysis.

### Results

Of the 114 patients included in the study, the mean age of 52 men was 42±12 years. The number of women was 62, and the mean age was 44±13 years (Table 1). The mean NLR of the groups was calculated (Table 1 and Figure 1) and the threshold value of NLR was taken as ≥1.8. Sensitivity, specificity, positive predictive and negative predictive values on NLR were calculated (Table 2 and Figure 1). There was no statistically significant difference between the groups in terms of age and gender. NLR increased as the degree of fibrosis increased (Figure 1), but this was not statistically significant. It was determined that sensitivity and specificity were low, and positive or negative predictive values were not significant (Table 2).

**Table 2:** Statistical Analysis of the Study Groups.

	Group 1 Fibrosis 1 – 2 n: 21	Group 2 Fibrosis 3 – 4 n: 75	Group 3 Fibrosis 5 – 6 n: 18	Specificity	Sensitivity	Positive predictivity	Negative predictivity	P value
NLR	1.4 ± 0.4	1.8 ±0.9	2.1±1.0	%58.5	%43.73	1.06	0.9	P= 0.69



**Figure 1:** NLR increase rate between the groups.

### Discussion

Chronic viral hepatitis B disease is an important health problem in our country and all over the world. Hepatitis B virus can progress to chronic inflammation, necrosis and fibrosis in the liver. Lympho-mononuclear cells play an important role in the liver fibrosis process. Leukocytes – neutrophils and lymphocytes constitute approximately 41 – 73% and 19 – 44% of total blood count respectively.

The presence of a systemic infection or systemic inflammatory response may cause an increase in the number of neutrophils and lymphocytes in the blood [5,6]. The use of NLR as a new marker of systemic inflammation has been proposed in various studies. In a large retrospective study conducted by Aydın, et al. the mean NLR between the age of 30 – 59 years was 1.8 – 2.0 [7]. In our study, the threshold value of NLR was ≥1.8, taking into account the mean age range of our

patients. Alkhouri, et al. found a correlation between NLR and the degree of liver fibrosis in non-alcoholic fatty liver patients and stated that NLR could be used as a marker in showing disease progression [8]. Asil m, et al. NLR was found to be increased in patients with steatohepatitis, and it was determined that this increase was probably due to inflammation in the liver and accompanying low-level systemic symptoms. thought to be due to inflammation [9]. Kuzu, et al. found no correlation between the degree of fibrosis and NLR in patients with chronic hepatitis C [10]. In a retrospective study conducted by Çelik, et al. no correlation has been detected between the fibrous score and NLR of chronic hepatitis B patients [11]. Yeşil, et al. determined that there was a correlation between liver fibrous grade and NLR in 286 chronic hepatitis B patients [12]. In our study, the NLR of the groups increased as the fibrous degree progressed (Figure 1), but it was not statistically significant. It was determined that the sensitivity and specificity of NLR were low for the groups, and there was no significant correlation between positive or negative predictive values.

## Conclusion

In conclusion, the calculation and use of NLR as a non-invasive test in estimating the liver fibrosis degree of chronic hepatitis B patients did not provide beneficial outcomes in the current research. Further controlled, prospective studies is required on this subject.

## Ethics Committee Approval

Ethics committee approval was not obtained because our article was a case report.

## Informed Consent

Consent was obtained from the patient for the procedure and publication.

## Declaration of Interests

There is no conflict of interest in publishing the article.

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