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A Study of Relationship between Fibrosis Level and Blood Neutrophil to Lymphocyte Ratio in Chronic Hepatitis B Patients

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Abstract
Background: *Liver fibrosis is an inevitable process in CHB. Many inflammatory cytokines, such as transforming growth factor-beta (TGF-beta) and platelet-derived growth factor, have been shown to activate hepatic stellate cells and result in advanced extracellular matrix deposition, which will eventually lead to liver fibrosis. The neutrophil to lymphocyte (N/L) ratio is a noninvasive and inexpensive marker of inflammation which can be simply acquired from the complete blood count. This marker combines data from two distinct pathways, lymphocytes which portray the regulatory pathway and neutrophils which cause ongoing inflammation.*
Methods: *The study was conducted on patients with Chronic Hepatitis B infection admitted in GEMS hospital. The study population was 50 patients and all were subjected through history, clinical examination and laboratory. The data were then analysed and appropriate statistical analysis was done.*
Results: *The study showed that patients with Fibrosis (Stages 3 & 4), correlated with Mean Neutrophil Lymphocyte ratio was proven to be statistically significant. NLR correlates positively with FIB – 4.*
Conclusion: *The NLR value is higher in HBV patients than in healthy individuals. It can be used as a predictive factor of disease severity in patients with chronic HBV.*

Introduction

- More than 350 million humans globally suffer from chronic hepatitis B virus (CHB) infection. Assessment of the degree of liver fibrosis is crucial for prognostic and therapeutic decisions in patients with CHB.
- Liver biopsy is currently the gold standard for estimating the seriousness of liver fibrosis
- Non-invasive methods such as the Fibro Test, mean platelet volume, FibroIndex and Hepascore are now favorable as an alternative to liver biopsy for predicting

liver fibrosis. However, some of these methods are not readily available and are not cost-effective.

- Liver fibrosis is an inevitable process in CHB. Many inflammatory cytokines, such as transforming growth factor-beta (TGF-beta) and platelet-derived growth factor, have been shown to activate hepatic stellate cells and result in advanced extracellular matrix deposition, which will eventually lead to liver fibrosis.
- The neutrophil to lymphocyte (N/L) ratio is a noninvasive and inexpensive marker of inflammation which can be simply

acquired from the complete blood count. This marker combines data from two distinct pathways, lymphocytes which portray the regulatory pathway and neutrophils which cause ongoing inflammation.

Aim of the Study

- To determine the association between the Neutrophil Lymphocyte ratio and the severity of liver fibrosis in patients with CHB infection.

Materials & Methods

- This was a prospective, observational study carried at GEMS hospital; department of General medicine, Srikakulam, India from November 2020 to June 2021 and follow up for 3 months.
- All data collected as part of the routine clinical care in hospitalized patients, which includes demographics, medical history, laboratory findings like CBC, LFT, viral markers, liver biopsy, coagulation profile, Alpha fetoprotein (AFP), radiology, procedural findings including medications.

Inclusion Criteria

1) Age of the patient's $\geq$ 36 years
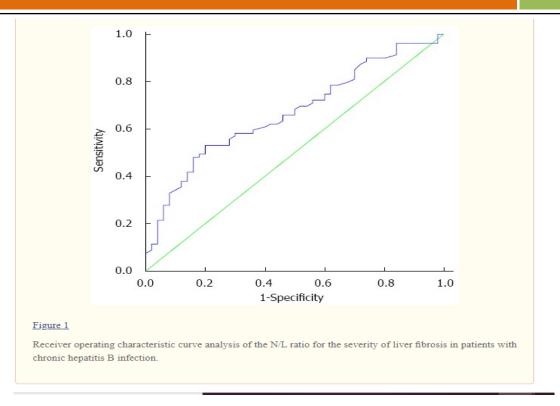2) Patients with chronic hepatitis B infection.

Exclusion Criteria

1) Patients with less than 36 years of age
2) Patients with HCV, HIV.
3) Patients with autoimmune diseases.
4) Patients receiving the blood transfusion products.
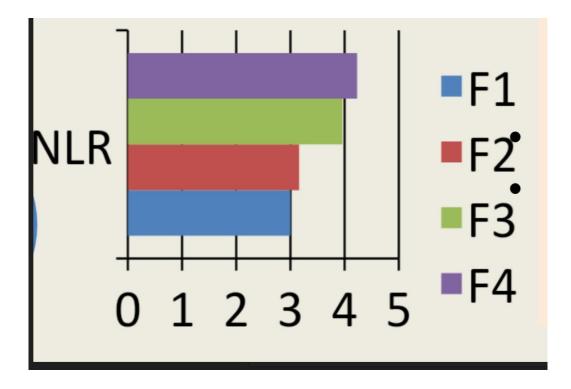5) Patients with Decompensated chronic liver disease.

Statistical Analysis

- For descriptive statistical analysis, mean, standard deviation, and frequencies were calculated.

- Different characteristics were represented as numbers or percentage wherever required. Statistical analysis was done by statistical software SPSS for Windows v21.0
- *P-Value* shows statistical significance when it was < 0.05.
- The stage of fibrosis was measured using a 4 point scale. the total wbc count, neutrophil and lymphocyte counts were recorded and NLR was calculated.
- In one year period total of 50 chronic hepatitis B patients were identified.
- The mean age of the patients was 36years (34 males and 16 females). After evaluating the biopsy samples in accordance with the METAVIR scoring system, the liver fibrosis stage was F0-F2 were 22 and mean NLR was 3.12; F3-F4 were 28 and mean NLR 4.1(p=0.02)

- n=50
- sex   male/female   34/16
- median age   36 years
- White blood cell ($\times$ 103 μL) 6300 (5400-7400)
- Platelet ($\times$ 103 μL) 217000 (180000-266000)
- Red blood cell distribution width 13.2 (12.5-13.5)
- Mean corpuscular volume 89.2 (85-91.3)
- Platelet distribution width 15.8 (12.9-16.3)
- Aspartate aminotransferase (U/L) 41 (28-67)
- Alanine aminotransferase (U/L) 54 (33-99)
- HBeAg (+) 37
- HBVDNA (IU/mL) 676500 (89000-13113084)
- Histology activity index 6 (4-8)
- Fibrosis
- 0   37 (28.7)
- 1   42 (32.6)
- 2   19 (14.7)
- 3   26 (20.2)
- 4   5 (3.9)

Figure 1

Receiver operating characteristic curve analysis of the N/L ratio for the severity of liver fibrosis in patients with chronic hepatitis B infection.

- Outcome – Neutrophil lymphocyte ratio correlates positively with FIB-4(r=0.36)

Results

- In one year period total of 50 chronic hepatitis B patients identified out of which males were 34 and females were 16.
- Patients with F0-F2 Fibrosis were 22 and mean Neutrophil Lymphocyte ratio(NLR) was 3.12

- F3- F4 fibrosis were 28 and mean Neutrophil Lymphocyte ratio(NLR) was 4.1 and p=0.02
- Mean FIB-4 among chronic hepatitis patients was 5.43
- NLR correlates positively with FIB-4(r=0.36)

Discussion

When patients with chronic hepatitis B are first seen in the outpatient clinic, we determine an algorithm. Generally, the main indicator of this algorithm is the viral load level, and patients with low viral load are usually monitored, while patients with high viral load are more commonly considered for liver biopsy.

In recent years, the NLR has become popular as a simple, inexpensive, and effective marker associated with various inflammatory and neoplastic diseases. In light of these studies, we aimed to investigate the relationship between fibrosis level and NLR for determining disease severity and making treatment decisions.

- A significant correlation was determined between fibrosis score and NLR (r: +0.36 p: 0.02); We demonstrated that there was a positive relationship between degree of fibrosis and NLR
- NLR, which reflects the inflammatory status of the patient, has been used as a simple, affordable, and easily accessible marker to predict prognosis in a variety of inflammatory and neoplastic diseases, such as ulcerative colitis, Crohn's disease, acute pancreatitis, colorectal cancer, breast neoplasms, lung cancer, hepatocellular carcinoma.
- Many studies have evaluated NLR as a noninvasive diagnostic model of hepatic fibrosis in different types of chronic liver disease. A recent paper by Alkhouri et al. shows that NLR is elevated in patients with nonalcoholic steatohepatitis (NASH) and significant fibrosis compared with patients who without NASH .

Conclusion

- The NLR value is higher in HBV patients than in healthy individuals. It can be used as a predictive factor of disease severity in patients with chronic HBV.

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