Evaluating the correlation between Neutrophil-to-Lymphocyte Ratio (NLR) and Child-Turcotte Pugh (CTP) Score for predicting the severity of Decompensated Liver Cirrhosis

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Abstract
Background: The Neutrophil-to-Lymphocyte Ratio (NLR) is a ratio used as a marker of ongoing inflammation and is associated with poor clinical outcomes in patients with liver cirrhosis. **Aims and objectives:** To determine the correlation between NLR and Child-Turcotte Pugh (CTP) score among decompensated liver cirrhosis patients in a tertiary care center. **Materials and methods:** A hundred patients with liver cirrhosis (age >18 years) were studied in the Department of Medicine, Gandhi Medical College, Bhopal, from June 2019 to July 2020. Complete blood count and laboratory findings for random and fasting samples were tested and recorded. An NLR was obtained. Child-Pugh Turcotte Score was used to evaluate the severity of liver cirrhosis in Class A (5-6), Class B (7-9), or Class C (10). **Results:** The majority of the liver cirrhosis patients were males (70%). On person correlation, NLR had a significant positive correlation with CTP score (r=0.572; p=0.002). **Conclusion:** A significant association was reported between NLR and CPT in assessing the severity of liver cirrhosis. Further research is required before the NLR ratio's potential as a mortality and prognosis predictor can be fully recognized.
Keywords: Child-Pugh Turcotte Score, Neutrophil-to-Lymphocyte Ratio, liver cirrhosis, inflammation

Introduction

End-stage liver cirrhosis occurs when healthy liver tissue is replaced by abnormal connective tissue, and nodules are formed in it. (Verhelst X 2016) Hepatitis B and C virus are two of the most common causes of liver cirrhosis. (Kwon YC 2014) It is estimated that cirrhosis and chronic liver disease induce disability in 31 million people worldwide. (Mokdad AA 2014)

This is why a scoring system must be used in a primary care setting to predict the outcome and severity of cirrhosis. Child-Turcotte Pugh score, can be used to predict the severity of liver failure based on five variables (bilirubin level, albumin concentration, INR, ascites volume, and hepatic encephalopathy). It is possible to determine the severity of the liver failure and the priority for liver transplantation, quality of life, and the outcome by using the Model for End-stage Liver Disease (MELD).

The neutrophil to lymphocyte ratio (NLR) is a simple biomarker for predicting systemic infection. (Biyik M 2013) It is possible to use NLR as an accurate prognostic marker for the severity of the infection or several types of malignancies. (Liu D 2017) Bacterial infections are associated with low lymphocyte levels, while high neutrophil levels are related to chronic inflammation. (Chen SS 2016) One of the hallmarks of liver disease is necroinflammation, which is particularly prevalent in advanced cirrhosis.

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(Chen SS 2016) Because of this, NLR can provide information about the severity of hepatocyte damage during fibrosis development. It is possible to use NLR and CTP to predict a poor outcome. Our study aimed to determine whether there was a significant correlation between high NLR ratios with the severity of decompensated liver cirrhosis based on CTP score; as this was a point-time approach study, the information related to the prognosis was not noted.

Materials and Methods

The present study was performed in the Department of Medicine, Gandhi Medical College, Bhopal, from June 2019 to July 2020.

Fifty patients with age above 18 years and not having any major condition including malignancy, blood transfusion in the last three months, HIV positive, diabetes mellitus, dyslipidemia, acute liver failure, autoimmune disease, and pregnancy, because it could affect the laboratory result particularly leukocyte count were included. The medical record registry of the patients was used to conduct a thorough assessment of medical history.Complete blood count and laboratory findings (e.g., complete blood count; liver function tests; electrolyte; glucose level; albumin; globulin; viral marker; and hemostasis function tests) were tested and recorded for both random and fasting samples. An NLR was then obtained by combining the levels of neutrophils and lymphocytes. It was determined how severe the liver cirrhosis was by using the Child-Pugh Turcotte Score. Class A (5-6), Class B (7-9), or Class C (10) are the three categories on a scale of 5 to 15 points (10-15). An online calculator (https:// www.mdcalc .com /child-pugh-score-cirrhosis mortality/) was used to calculate the CTP score.

SPSS Inc.'s version 25.0 was analyzed using the Kruskal-Wallis test for statistical analysis because the data were not normally distributed. A chi-square test was used for the categorical variable, gender, to determine any significance in the three groups because the data were not normally distributed. The Spearman correlation test was used to

examine the relationship between NLR and the severity of liver cirrhosis based on the Child-Turcotte Pugh score.

Results

In a present cross-sectional observational study, 50 patients with liver cirrhosis were studied. Out of 50 patients with liver cirrhosis, 35 (70%) were males, and 15 (30%) were females.
Table 1 shows the baseline characteristics of the study population. They were serologically testing revealed that the most common infection was the hepatitis B virus (48%).

Table 1: Baseline characteristic of the 50 liver cirrhosis patients

Characteristics	Patients with liver cirrhosis (n=50)
Gender (male/female)	35/15
Age (years)	54.24±8.62*
Hemoglobin (g/dL)	8.62±2.34*
Platelet count (x109 /L)	126.0 (24.0-582.0)
Serum Iron (μg/dL)	31.0 (9.0-274.0)
Total Iron Binding Capacity/TIBC (μg/dL)	181 (35-408)
Ferritin (ng/mL)	388.28 (2.4-10342)
Prothrombin Time (secs)	19.2 (11.8-45.8)
INR	1.29 (0.78-2.72)
Total bilirubin (mg/dL)	1.34 (0.31-32.7)
Urea (mg/dL)	32.4 (7-268)
Creatinine (mg/dL)	0.93 (0.52-13.58)
Albumin (g/dL)	2.2 (1.5-3.7)
Child Turcotte Pugh score	9 (5-12

INR: International normalised ratio. Data s expressed as median (interquartile range) or *mean ± standard deviation

Patients were divided into three groups based on NLR and NLR ≤2.0, 2<NLR<5, and NLR ≥5. A comparison of demographic and laboratory parameters was performed as depicted in table 2. Though no significant difference was obtained between laboratory findings and NLR, age, albumin, creatinine, bilirubin, and CTP score were higher in patients with NLR ≥5. On person correlation, it was revealed that NLR had a significant positive correlation with CTP score (r=0.572; p 0.002).

Table 2: Comparing Clinical and laboratory findings of 50 patients liver cirrhosis

Parameters	NLR ≤2 (n=6)	2<NLR<5 (n=24)	NLR ≥5 (n=20)	P-value
Age (years)	52.82±17.42	51.89±14.62	52.26±10.25	0.782
Gender (Male/Female)	3/1	16/9	15/6	0.664
Albumin (g/dL)	2.4 (1.4-3.2)	2.63 (1.2-3.9)	2.4 (1.2-2.9)	0.621
INR	1.48 (1.1-1.92)	1.31 (0.58-1.98)	1.31 (1.25-2.68)	0.621
Creatinin (mg/dL)	0.88 (0.6-0.94)	0.86 (0.53-6.62)	1.51 (0.52-13.58)	0.128
Total Bilirubin (mg/dL)	1.01 (0.8-2.2)	1.42 (0.35-7.82)	1.6 (0.32-31.2)	0.323
CTP score	8 (7-10)	8.5 (5-11)	9 (7-13)	0.131

Discussion

This cross-sectional study was conducted to determine a statistically significant correlation between NLR and CTP scores. A correlation between NLR and the ChildTurcotte Pugh score was found in the study; thus, the scoring system could be used as a severity predictor among decompensated liver cirrhotic patients. It shows that patients with a high NLR value are more likely to have a high CTP score. Five factors make up the CTP score, each of which significantly impacts the prognosis of patients with cirrhosis. (Tanoglu A 2014, Kim HJ 2013)

When He et al. (He Q 2014) compared patients with compensated cirrhosis, NLR was higher in the decompensated group. A complex relationship between systemic inflammation and the immune system has been suggested for advanced or decompensated cirrhosis. (Arroyo V 2015) The immune system will recognize a damaged hepatocyte's ligands, known as damage-associated molecular patterns (DAMPs), in compensated cirrhosis. (Dirchwolf M 2015) Sterile systemic inflammation is the condition's result. On the other hand, Decompensated cirrhosis causes ligands produced by bacterial translocation or the bacterial component to be shifted into circulation via static portal circulation and the deterioration of the gut wall. (Martínez-Esparza M 2015)

Ongoing systemic inflammation can be indicated by high neutrophil levels and lymphocyte levels associated with the release of endotoxin from a pathogenic organism [28-30]. (Zubieta-Rodríguez R 2017, Kalra A 2017) The neutrophil-to-lymphocyte ratio (NLR) is a ratio of neutrophils to lymphocytes, linked to several diseases, including autoimmune and other conditions. (Riley LK 2015). The clinician could make the time-saving and non-invasive interpretation directly, so its applicability in daily clinical practice is specific. (Peng Y 2018) There are many reasons why it's essential to identify patients with a high NLR. According to a study published in PLoS One, there is a strong correlation between NLR and the cirrhosis stage, as well as liver-related death in patients with decompensated liver cirrhosis.

A new prognostic factor for prioritizing liver transplant patients has been proposed by Leithead JA et al. (Leithead JA 2015)

According to the authors' knowledge, Probowati W et al. conducted the first correlation study of NLR and CTP score among cirrhotic patients in Indonesia and found that NLR positively correlated with CTP score among 33 patients. (Probowati W 2016) According to the findings of Biyik M et al., NLR is an independent predictor of mortality in Cox regression models (r=0.25; P=0.002). (Biyik M 2013) In a different population of patients with HCC, NLR was found to have a linear relationship with CTP score as a prognostic factor for hepatocellular carcinoma (HCC). (Oh BS 2013) The one-month survival rate among CTP class C patients was significantly higher in patients with high NLR, as demonstrated by Kwon JH et al. (Kwon JH 2015)

Limitations were imposed on the study. Several variables were measured using a point-time approach. A confounding factor could affect the NLR value by cross-sectional measurements of the outcome and laboratory results.

Conclusion

NLR and CTP scores have a positive correlation, according to the study. NLR could indicate systemic inflammation, but cytokines may

play a specific role in the inflammatory process itself (not measured in the study).

It is unclear whether or not a CTP score can be used to predict severity without reference to NLR. For high-NLR patients to progress to the decompensated stage, NLR threshold levels and confounding conditions must be determined in future studies, including cohort studies. As a result, regardless of CTP, a high NLR value could be used to predict death in decompensated liver cirrhotic patients.

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