ORIGINAL RESEARCH PAPER

General Medicine

A STUDY OF BLOOD NEUTROPHIL TO LYMPHOCYTE RATIO AS A PROGNOSTIC MARKER IN LIVER CIRRHOSIS

KEY WORDS: NLR ,CTP , Cirrohosis

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ABSTRACT

Introduction: Neutrophil to lymphocyte ratio (NLR) is used as marker of ongoing inflammation process and raised NLR has been associated with poor clinical outcomes among liver cirrhosis patients. Necroinflammation is one of the hallmarks of liver disease particularly in advanced cirrhosis. Therefore, NLR is able to provide the information related to severity of damaged hepatocyte during fibrosis formation. **Aim and Objective:** To study neutrophil to lymphocyte ratio as a prognostic marker in liver cirrhosis and association between NLR and CTP score. **Methodology:** This was a hospital based prospective observational study, started after approval from institutional research review board, from March 2020 to October 2021. Sample size was 100. The study subjects were patients with liver cirrhosis undergoing inpatients and outpatients care in our hospital, that meets the inclusion and exclusion criteria. Blood tests were done to measure NLR and CTP score. Statistical analysis was carried out to determine the Pearson correlation between NLR and CTP score. **Results:** This study was conducted on 100 cases. In our study out of 100 cases, 77 were male and 23 were female, mean age was 44.6, major etiology was ethanol related cirrhosis, mean NLR was 7.9, mean CTP score was 10.9. A significant correlation between NLR and CTP score was obtained (p=<0.0001) and it was positively correlated (r=0.75). **Conclusion:** Raised NLR is strongly associated with complications and short-term mortality in patients with liver cirrhosis. Based on this study, it can be concluded that NLR and CTP score has a positive correlation. Therefore, high NLR value could be used as prognostic marker and can assist in early detection of decompensation in cirrhotic patients.

INTRODUCTION

Cirrhosis is generally known as an end-stage process where healthy normal liver tissue is replaced by the abnormal connective tissue, and it induces nodule formation in it. [1,2]Neutrophil lymphocyte ratio is one such inexpensive and easily available marker of systemic inflammation. Neutrophil count helps in identifying ongoing inflammation and lymphocyte count represents immune regulatory pathway. Therefore, NLR is able to provide the information related to severity of damaged hepatocyte during fibrosis formation. Studies have shown NLR to be useful in predicting outcome and mortality in patients with viral hepatitis, hepatocellular carcinoma, liver transplantation and non-alcoholic fatty liver disease. Both NLR and CTP might be used to predict poor outcome independently.

OBJECTIVES:

To study association between NLR and Child-Turcotte Pugh (CTP) score in liver cirrhosis.

MATERIALS AND METHODS

The study was conducted at Sawai Man Singh Medical College & Attached Hospitals, Jaipur, Rajasthan, from March 2020 to October 2021 . It was a prospective observational study.Patients diagnosed with Liver cirrhosis were included in the study.

Inclusion Creteria:

Liver cirrhosis, diagnosed via USG along with supporting history, clinical and laboratory finding.

Exclusion Criteria:

Any condition that may affect NLR at time of assessment, like HIV, cancer ,Infection Pregnancy and lactation.

METHODOLOGY

Patients attending the Medicine and Gastroenterology outpatient and inpatient department, who are known cases of cirrhosis of liver inspite of etiology, who full-fill the inclusion and exclusion criteria were involved in the study after obtaining informed consent from the patients.

Blood samples from these patients were taken and sent for investigations. The investigations includes, CBC and their neutrophil to lymphocyte ratio was calculated and and the severity of liver cirrhosis was evaluated using CTP Score.

Statistical Analysis

Data was feeded in Excel Sheet. Qualitative data was presented as percentage and proportion..

Chi-square test was used to analyze nonparametric or categorical data. For analysis of ordinal scale data, Students t-test was used. Karl–Pearson correlation coefficient was calculated to observe correlation between variables. $P < 0.05$ was taken as significant and <0.01 as highly significant. Appropriate statistical tool was used for analysis.

RESULTS:

We conducted this study on 100 cases and out of 100 patients we observed that majority (60%) of patients were in age group 36-55 years followed by 22% in age group 15-35 years followed by 18% in age group 56-75 years. The mean age for our study group was 44.62 years.

In our study majority (77%) of patients were male. In our study 59% patients were alcoholic and major etiology presented in our study was ethanol related (58%) followed by cryptogenic (22%) followed by hepatitis B related (11%) followed by autoimmune followed by hepatitis C related.

While investigating blood samples we observed that mean total leucocyte count was 6.89, mean neutrophil was 81.30, mean Lymphocyte was 12.6, mean Bilirubin was 6.46, mean albumin was 2.67, mean PT was 30.63 and mean INR was 2.41.

We distributed NLR into subcategory. Majority (44%) patients were in 6.1-9 group followed by 20% in 3.1-6 NLR group followed by 14% in 9.1-12 NLR group followed by 13% in >12 NLR group followed by 9% in 1-3 NLR group. Mean NLR for our study group was 7.9. We correlated NLR ratio with Age group. We found that 28% of study population with age group 36-55 years were having NLR 6.1-9 followed by 13% patients of

same age group with 3.1-6 NLR. Here we analyzed that higher NLR was found in middle age group patients.

We documented that 30% patients in NLR group 6.1-9 were of ethanol related. We can say that ethanol related patients shows more variation in NLR ratio followed by cryptogenic cirrhotic patients followed by Hepatitis B related cirrhotic patients. We observed that 67% patients were of CTP Class C followed by 22% patients of CTP Class B. We also found that as CTP Class increases mean NLR also increase with mean NLR in CTP Class A, Class B and Class C was 2.85, 6.13 and 9.42 respectively. The p value was <0.0001. In our study majority (68%) patients were of CTP Score >9 followed by 21% patients with 7-9 CTP Score. Mean CTP Score in our study was 10.9.

Table 1: Distribution of cases according to CTP Class and correlation of NLR with CTP class.

Parameter	Class A		Class B		Class C		Total
	No. of Patients	Percentage	No. of Patients	Percentage	No. of Patients	Percentage	
	11	11	22	22	67	67	100
NLR Mean±SD	2.85±0.84		6.13±2.6		9.42±3.08		<0.0001

We distributed cases according to CTP Class A, B, and C. We analyzed that 67% patients were of CTP Class C followed by 22% patients of CTP Class B followed by 11% patients of CTP Class A. We also found that as CTP Class increases mean NLR also increase with mean NLR in CTP Class A, Class B and Class C was 2.85, 6.13 and 9.42 respectively We correlated NLR ratio with Age group. We found that 28% of study population with age group 36-55 years were having NLR 6.1-9 followed by 13% patients of same age group with 3.1-6 NRL.Here we analysed that higher NLR ratio was found in middle age group patients.

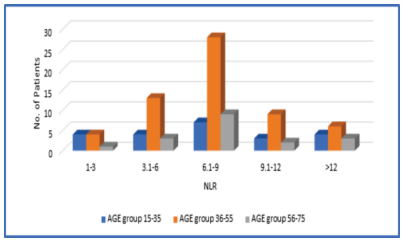

Figure 1 : Correlation of NLR with Age distribution.

We observed that 30% patients in NLR group 6.1-9 were of ethanol related. We can say that ethanol related patients shown more variation in NLR ratio followed by cryptogenic etiology.

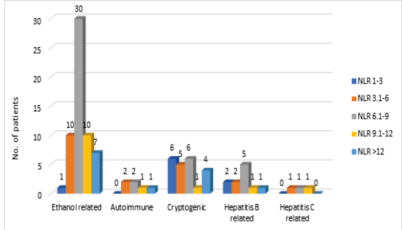

Figure 2:- Correlation of NLR with etiology

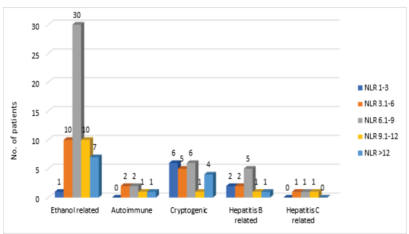

Table 2 : Correlation of NLR with complications

NLR	COMPLICATIONS				
	Esophageal varices	Hepatic encephalopathy (HE)	Hepato-renal syndrome (HRS)	Ascites	None
1-3	7	0	0	2	2
3.1-6	15	1	0	13	0
6.1-9	37	20	2	39	1
9.1-12	12	12	3	14	0
>12	11	12	0	12	0

We distributed cases according to complications and found that 82% patients were of esophageal varices followed by 80% patients of ascites followed by 45% of patients were of HE. Out of 100 patients, we found that 11% patients were of HE Grade 1 and 14% patients with HE Grade 2 and 12% patients with HE Grade 3 and 8% patients with HE Grade 4.

Table 3: Pearson Correlation of NLR with CTP Score.

	CTP Score	
NLR	r	P-value
	0.7508	<0.0001

We correlated NLR Ratio with CTP Score. We documented r value to be 0.75. The p value was <0.0001. This shows that there was significant difference found as p-value was <0.05. This study shows that NLR and CTP score has a positive correlation.

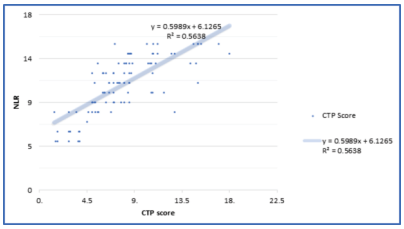

Figure 3:- Pearson Correlation of NLR with CTP Score.

DISCUSSION

Blood Leucocyte count has previously been used as a surrogate marker for sepsis. However, in patients with cirrhosis it is difficult to make a diagnosis of infection solely based on leucocyte count as it has its own drawbacks. Once a patient develops infection the total count is bound to rise. However, there are evidence which say in 50% bacteremia total count can be normal.[3] Hence there is no consensus for a leucocyte cut-off point for diagnosing infection.

NLR was found higher among decompensated patients compared to the compensated cirrhosis patients in a study conducted by He et al[4].

In general,high neutrophil levels could indicate on-going systemic inflammation while lymphocyte level positively correlated with endotoxin released by the pathogenic organism and cirrhotic severity[5]. NLR is ratio of neutrophil and lymphocyte, its levels are associated with certain conditions including autoimmune and other diseases[6], this also could be a limitation of NLR use in general population. Nevertheless, its applicability on daily clinical basis is certain since the time-saving and non-invasive interpretation could directly be made by clinician[7].

In our study majority (60%) of patients were in age group 36-55 years followed by 22% in 15-35 years. The mean age for our study group was 44.62 years.77% patients were male in our study.

A similar study by Vineeth V K et al[8] found that Mean age for the cohort was 53.91±10.9 with maximum patients between the age group 51-60 (38.3%). Out of 120 patients there were 108 male and 12 females. Zhang H et al[9] found that mean age for

their study group was 53.2 years and out of 148 patients there were 118 males.

We observed that 59% patients were alcoholic and 11% patients were of hepatitis B followed by 3% patients of hepatitis C. In our study 58% patients were of ethanol related followed by 22% of cryptogenic followed by11% patients of hepatitis B related.

Mishra D et al[10] found that alcohol was the major cause of cirrhosis of liver in this region. Multiple studies from different centers of India have reported alcohol to be the commonest cause of cirrhosis with prevalence ranging from 30% to 70% of all cases of cirrhosis.[11]

In our study mean TLC, neutrophil, Lymphocyte, Bilirubin, albumin, PT and INR was 6.89, 81.30, 12.6, 6.46, 2.67, 30.63 and 2.41 respectively. We distributed NLR into subcategory. Majority (44%) patients were in 6.1-9 group followed by 20% in 3.1-6 NLR group. Mean NLR for our study group was 7.9. We found that 11% patients were of HE Grade 1 and 14% with HE Grade II and 12% patients with HE Grade 3 followed by 8% with HE grade IV.

Fan Z et al[12] found that alanine aminotransferase (ALT), bilirubin, ammonia, hemoglobin, alpha fetoprotein (AFP) and the rate of antiviral therapy were higher, and age, creatinine and NLR were lower in the ALSS group than in the SOC group.

In our study 82% patients were of esophageal varices followed by 80% patients of ascites, 45% of patients were of HE. Vineeth V K et al[13]found that total of 34 (28.3%) patients had cirrhosis with portal hypertension without evidence of esophageal varices and were categorized a compensated cirrhosis. Among the decompensated Cirrhosis, 47 (39.2%) patients had esophageal varices with evidence of bleeding and 39 (32.1%) patients had cirrhosis with hepatic encephalopathy and spontaneous bacterial peritonitis (SBP) as complications. Mean NLR for the patients was 5.824±5.632 (95% CI 4.81- 6.84).

Patients were divided into 5 groups on basis of NLR. Twenty-one Patients (42%) with NLR of 1-3 had compensated cirrhosis. It was observed that as the NLR increased, percentage of patients with decompensated cirrhosis also increased and 11 patients (91.7%) with NLR >12 had decompensation. It was also noticed that as the NLR increased, the incidence of complications also increased with 66.7% of patients with NLR >12 having more than 2 complications that is hepatic encephalopathy and SBP .

We observed that majority (68%) patients were of CTP Score >9 followed by 21% patients with 7-9 CTP Score. Mean CTP Score in our study was 10.9. In our study 67% patients were of CTP Class C followed by 22% patients of CTP Class B. In our study we documented that mean NLR in CTP Class A, Class B and Class C was 2.85, 6.13 and 9.42 respectively. The p value was <0.0001. There was significant difference found as p value was <0.05. By logical regression we correlated NLR Ratio with CTP Score. We found r value to be 0.75. The p value was <0.0001. This shows that there was significant difference found as p-value was <0.05.

Sungkar T et al[9] found that CTP score was higher in NLR ≥5 group patients. In addition, a significant correlation between NLR and CTP score was demonstrated in their study (r=0.326; p 0.008) using Spearman correlation test.The exact mechanism of NLR to explain its association with prognosis and correlation with CTP score remains elusive.[14]

CONCLUSION

Raised Neutrophil to Lymphocyte Ratio is strongly associated with complication and short-term mortality in patients with cirrhosis. Based on the study, it can be concluded that NLR and CTP score has a positive correlation.Therefore, high NLR value could be used as prognostic marker and can assist in early detection of decompensation in these patients, regardless of CTP score.

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