

## A study of NLR and it's correlation with severity and complications of liver cirrhosis on the basis of child turcotte pugh score in a tertiary care hospital, Vijayapur

Appuraj Tandale<sup>1</sup>, M.M. Kalburgi<sup>2</sup>, Nasiruddin R. Itagi<sup>2\*</sup>, Raghavendra Khanapur<sup>2</sup> and Santosh Pattar<sup>2</sup>

<sup>1</sup>Department of General Medicine, M.S. Ramaiah Medical College, M.S. Ramaiah Nagar, MSRIT Post, Bengaluru-560054, Karnataka, India and <sup>2</sup>Department of General Medicine, Al Ameen Medical College and Hospital, Athani Road, Vijayapur-586108, Karnataka, India

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**Abstract:** *Aim and Objectives:* To obtain NLR from complete blood count in patient with liver cirrhosis, to perform Liver function test and clinical examination and obtain CTP score in patient with liver cirrhosis and to evaluate the role of NLR and its correlation with severity and complications of liver cirrhosis on the basis of Child Turcotte Pugh score. *Methods:* It is a prospective observational study of 90 patients who fulfill inclusion and exclusion criteria and were followed up for one year, evaluated with investigations, includes hematological investigations, ascitic fluid analysis, ultrasound abdomen. Patients who developed complications were identified and correlation with already calculated NLR was done and results were analysed. *Results:* The blood samples of 90 cirrhosis patients were collected and analysed for NLR and CTP. Out of these patients 20% developed upper GI bleed, 34.4% developed Ascites and 16.67% developed hepatic encephalopathy. There was a positive correlation found between NLR and CTP which was statistically significant ( $p=0.0001$ ). Patients with higher NLR were correlated to CTP class B and C thus showing a positive relationship with the severity of disease. *Conclusion:* This study reveals that there is a statistically significant correlation between NLR and CTP. NLR can be used as a single independent biomarker and simpler scoring system for assessment of severity of liver cirrhosis.

**Keywords:** Cirrhosis, Neutrophil to Lymphocyte Ratio, Child Turcotte Pugh Score.

### Introduction

Cirrhosis is the end stage of fibrosis of liver parenchyma which results in hepatic function alteration and nodule formations [1]. The healthy normal liver tissue is replaced by the abnormal, connective tissue, and it induces nodule formation in it [2-3].

Cirrhosis is most commonly caused by alcohol, hepatitis B, hepatitis C, and non-alcoholic fatty liver disease. Neutrophil to lymphocyte ratio (NLR) is stated as a simple biomarker which can be used to predict systemic infection or inflammation. The normal NLR values in an adult, non-geriatric, population in good health after a cohort study are between 0.78 and 3.53 and mean NLR being 1.65 [4]. Child Turcotte Pugh (CTP) is used to assess the prognosis in cirrhosis and to provide standard

criteria for listing a patient as a candidate for liver transplant [5]. CTP score consists of five indicators which relate to prognosis of liver cirrhotic patients [6-7].

Neutrophil-to-lymphocyte ratio (NLR) is a novel inflammation index. As emerging laboratory marker, NLR could be used as accurate prognostic marker to predict severity of the inflammatory process. High neutrophil level is associated with chronic inflammation while decreased levels of lymphocyte are linked with bacterial infection and regulatory scheme [8]. Necroinflammation is one of the hallmarks of liver disease particularly in advanced cirrhosis [9].

Therefore, during fibrosis formation NLR is able to provide the information related to

severity of damaged hepatocyte to correlate NLR with CTP score in patients with cirrhosis of liver. Study has been done on correlation between NLR and MELD score. But adequate study has not been done on NLR and CTP score and especially in southern India.

**Material and Methods**

The study was a Hospital based Cross-sectional Study on 90 patients done in tertiary care centre in Vijayapur over a period of 18 months ie Jan 2021 to June 2022. Patients aged above 18 years and diagnosed with liver cirrhosis on USG were included in the study. Patients with malignancy, blood transfusion in the last three months, HIV positive, DM patients, dylipidemia, acute liver failure, autoimmune disease and pregnancy,

Patients on immunosuppressive medications, patients with known renal disease, coronary artery disease, COPD or active infection were excluded from the study.

A detailed history taking and physical examination was performed on all patients. All base line investigations like complete blood count, liver function test, serum proteins, serum electrolytes, renal function test, PT, INR ascitic fluid analysis, ultrasound abdomen. Ultrasonography of liver was done to confirm the diagnosis. Neutrophil to lymphocyte ratio and Child Turcotte Pugh score were derived for every patient from the laboratory parameters Table-1 [10]. Written consent was taken from every patient.

**Table-1: Modified Child Pugh Score [10]**

Parameter	Assign 1 point	Assign 2points	Assign 3 points
Ascites	Absent	slight	Moderate
Bilirubin(mg/dl)	<2	2-3	>3
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time (second over control) or INR	<4	4-6	>6
	<1.7	1.7-2.3	>2.3
Hepatic encephalopathy	None	Grade1-2(Mild to moderate)	Grade 3-4(severe)

The severity of cirrhosis [10]:

- Child-Pugh A: 5 to 6 points
- Child-Pugh B: 7 to 9 points
- Child-Pugh C: 10 to 15 points

A - good hepatic function, B - moderately impaired hepatic function, and C - advanced hepatic dysfunction.

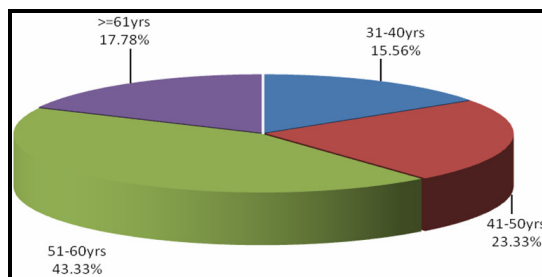
Statistical Analysis was done using SPSS version 22.0. P <0.05 will be accepted as significant

**Results**

The study population included 90 patients who have fulfilled the inclusion and exclusion criteria, Among 90 patients, 69 were males and 21 patients were females, predominant population is formed by males. This indicates prevalence pattern of cirrhosis in general population. Among the 90 pateints maximum patients ie 39 patients, were in the age group of 51-60 ,21 patients were

in the age group of 41-50 years.16 patients were in the age group of >61 years and 14 patients in the age group of 31-40 years [Figure 1]. Mean age of the population is 52.17±10 years.

**Fig-1:** Age wise distribution of patients



NLR is the ratio of absolute count of neutrophils to the absolute count of lymphocytes which is calculated by dividing absolute neutrophil count by absolute lymphocyte count. Maximum number ie 36

patients had an NLR of 2-4 followed by 28 patients with NLR <2 and 26 patients had an NLR of >4.1. Mean NLR is 3.52 [Table 2].

**Table-2: NLR levels wise distribution of patients**

NLR levels	No of patients	% of patients
<2.0	28	31.11
2.0-4.0	36	40.00
>=4.1	26	28.89
Total	90	100.00
Mean	3.52	

Among 90 patients, 18 patients developed upper gi bleed as a complication. It is seen that as the NLR increases, the number of patients having

upper GI bleed also increased. The complications were more prevalent in the higher NLR group, with a p value of 0.0030 (p <0.05).

31 patients developed ascites as a complication, which was more prevalent in the high NLR group, with a p-value of 0.0001 (p <0.05). 15 patients developed hepatic encephalopathy, which was also found to be more prevalent in the high NLR group, with a p value of 0.0010 (p <0.05) [Table 3] shows that patients with a higher NLR has a strong positive correlation with the prevalence of complications with a p value less than 0.05, which is statistically significant.

**Table-3: Association between NLR Levels and Complications**

Complications	<2.0	%	2.0-4.0	%	>=4.1	%	Total	%	$\chi^2$	p-value
<b>UGI bleed</b>										
Absent	26	36.11	31	43.06	15	20.83	72	80.00	11.8200	0.0030*
Present	2	11.11	5	27.78	11	61.11	18	20.00		
<b>Ascites</b>										
Absent	26	44.07	28	47.46	5	8.47	59	65.56	36.4800	0.0001*
Slight	2	7.41	7	25.93	18	66.67	27	30.00		
Moderate	0	0.00	1	25.00	3	75.00	4	4.44		
<b>HE grading</b>										
None	27	36.00	33	44.00	15	20.00	75	83.33	18.0100	0.0010*
Grade 1-2	1	12.50	1	12.50	6	75.00	8	8.89		
Grade 3-4	0	0.00	2	28.57	5	71.43	7	7.78		

**Table-4: Association between NLR Levels and Levels of CTP Grading**

CTP grading	<2.0	%	2.0-4.0	%	>=4.1	%	Total	%	$\chi^2$	p-value
Grade A	17	60.71	9	25	3	11.53	29	32.22	23.3810	0.0001*
Grade B	8	28.57	14	38.88	6	23.07	28	31.11		
Grade C	3	10.71	13	36.11	17	65.38	33	36.67		
Total	28	100	36	100	26	100	90	100.00		

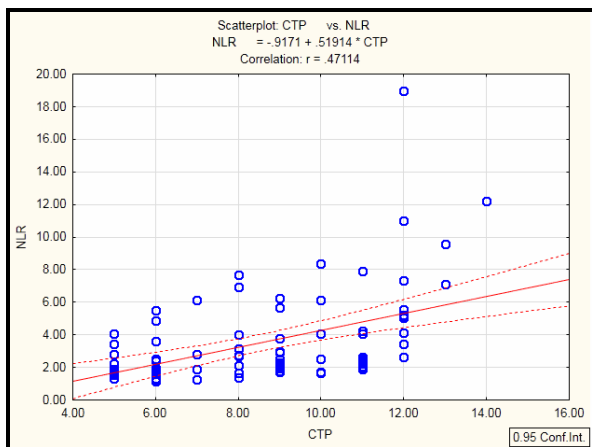
\*p<0.05

**Correlation between NLR and CTP:** Child turcotte pugh score was calculated using clinical parameters such as ascites and hepatic encephalopathy and laboratory parameters such as serum albumin, total bilirubin and INR. Out of 28 patients who had NLR <2, 17 patients ie (60.71%), belonged to CTP Grade A (5-6). Out of

36 patients who had NLR 2-4, 14 patients ie (38.88%), belonged to CTP Grade B (7-9) followed by 13 patients (36.11%) belonged to CTP Grade C (10-15), Out of 26 patients who had NLR >=4.1, 17 patients (65.38%) belonged to CTP grade C (10-15). There was a strong positive correlation between NLR and CTP

[Figure-2], which was statistically significant (p-value-0.0001) [Table 4].

**Fig-2:** Scatterplot depicting correlation between NLR and CTP



### Discussion

Liver cirrhosis is a diffuse process characterized by tissue fibrosis and conversion of normal liver architecture not structurally abnormal nodules [11]. It is a common end point of various causes of chronic liver diseases. The rate at which chronic liver disease transforms into hepatic cirrhosis is highly unpredictable and it depends upon a lot of factors, the most important of them being the cause of CLD.

The natural course of cirrhosis is characterized by compensated stage followed by a decompensated stage [12-13]. Transition to decompensated stage is marked by development of any of the following complications: variceal hemorrhage, ascites, hepatic encephalopathy and jaundice [12, 14]. These complications result from portal hypertension and /or from liver insufficiency. It was recently determined by consensus that compensated and decompensated cirrhosis should be considered separate disease entities.

The rate of transformation of compensated cirrhosis to decompensated state is highly variable and mainly depends on the cause of cirrhosis. There is an overwhelming evidence of role of inflammatory markers in pathogenesis of liver disease. Neutrophil to lymphocyte ratio is one such cost effective, readily available and easily calculated marker of systemic inflammation, as neutrophil count helps in

identifying ongoing inflammation and lymphocyte count represents immune regulatory pathway [15].

Studies have shown NLR to be helpful in predicting outcome and mortality un patients with viral hepatitis, hepatocellular carcinoma, liver transplantation and non alcoholic fatty liver disease [16-19]. Various studies have shown NLR as an important biomarker of ongoing inflammation and can reflect a persons immunity to liver cirrhosis.

Recently NLR has also emerged as a predictor of mortality independent of MELD score in patients with liver cirrhosis and with hepatocellular carcinoma as well as in candidates on liver transplantation lists [20-21]. CTP score consists of 5 indicators which also relates to the prognosis of liver cirrhotic patients [22-23]. NLR reflects systemic inflammation s well as immune dysregulation and has been previously shown to predict prognosis in stable patients (i.e without acute decompensation with end stage cirrhosis listed for liver transplanted) [24]. In the study conducted by He et al .NLR was significantly high in decompensated than in compensated cirrhotic patients [25].

In our study conducted at tertiary care hospital in Vijayapur, 76.67% were males and 23.33% were females. Among the study population maximum number of patients ie 43.33% were in the age group of 51-60 years. In our study maximum patients had NLR within 2-4. In a study conducted by Vineeth VK et al .he showed that the patients with high NLR had a positive correlation with complications, thereby was associated with higher short term mortality [26].

In our study, among 90 patients, 20% developed upper GI bleed, 34.4% developed Ascites and 16.67% developed hepatic encephalopathy. It was also seen that as the NLR increased, the number of patients with complications (UGI bleed, ascites, hepatic encephalopathy) also increased. All these complications had statistically significant relation with NLR.(p <0.05). In our study there was a strong positive correlation found between NLR and CTP which was statistically

significant ( $p=0.0001$ ). Patients with higher NLR were correlated to CTP class B and C thus showing a positive relationship with the severity of disease.

### Conclusion

It can be concluded from our study that there is a strong positive correlation between NLR and

CTP. This study reveals that cirrhosis patients with higher NLR have a high likelihood of developing complications. Therefore Blood neutrophil to Lymphocyte Ratio is a prognostic marker in liver cirrhosis. Thereby it can help in slowing the progression of the disease for early detection and timely intervention.

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\*All correspondences to: Dr. Nasiruddin R. Itagi, Assistant Professor, Department of General Medicine, Al Ameen Medical College and Hospital, Athani Road, Vijayapur-586108, Karnataka, India. E-mail: nasirri@gmail.com