ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 2, March - 2023, Page No. : 74 - 80

A study to evaluate the correlation of NLR with synthetic liver function in stable liver cirrhosis at a tertiary care hospital

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How to citation this article: Dr. Rakasi Raghudeep Reddy, Dr. P Tamilselvi, Dr. V M Jyotsnaa Grace, Dr. VR Mohan Rao, "A study to evaluate the correlation of NLR with synthetic liver function in stable liver cirrhosis at a tertiary care hospital", IJMACR- March - 2023, Volume – 6, Issue - 2, P. No. 74 – 80.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background and Objectives: Liver cirrhosis is defined as diffuse hepatic process characterized by fibrosis and conversion of normal liver architecture into structurally abnormal nodule.2 It is the final common pathway for all chronic liver diseases. Cirrhosis currently causes 1.16 million deaths making it the 11th most common cause of death.3,4 Various studies have shown NLR as an important biomarker of ongoing inflammation and can reflect a person's immunity to liver cirrhosis.13 In developing countries where resources are deficient, NLR is an ideal test for early detection of infection and inflammation. NLR has also emerged as a predictor of mortality independent of MELD scores in patients with cirrhosis and with hepatocellular carcinoma, as well as in candidates on the liver transplantation list. OBJECTIVE- To evaluate the Correlation of NLR with Liver function in liver cirrhosis patients.

Methodology: Cross sectional study, 100 patients attending the OPD of the general medicine were included. Patients who got admitted where thoroughly evaluated with investigations that includes- Complete Blood Count, Liver Function Tests, Serum Proteins, Renal Function tests, Coagulation Profile. The severity of the liver disease is evaluated by Child Turcotte-Pugh score. The scoring ranges from 5 - 15 points and the patients were categorised into three groups -class: A (5 - 6), B (7 - 9), and C (10 - 15). Continuous data will be expressed as means and standard deviation. Tests of significance used are Chi square test and one-way ANOVA test. Statistical analysis will be done by using SPSS version 26. Level of significance is taken as $p<0.05$.

Results: Among the study population 57% belong to least severe liver disease, followed by 27% belonged to moderately severe liver disease and 16% belong to most severe liver disease. Mean platlet count in study population among the NLR < 3 group was 132.34±9.54, in the 3≥ NLR ≤6 group was 127.53±9.69 and in the NLR > 6 group was 113.35 ± 10.42. Prothrombin time in patients in NLR < 3 group was 12.4±8.10, in the 3≥ NLR ≤6 group was 15.3±7.23 and in the NLR > 6 group was 19.5 ± 7.12.

Conclusion: It was concluded from the study that the NLR and CPS scores are significantly correlated. The laboratory parameters (mean ± SD) were tabulated into three groups according to the NLR score and correlation analysis was done. Significant correlations were observed between NLR scores and age, platlet count, prothrombin time, INR, Total bilurubin and serum albumin.

Introduction

One of the most significant and interesting organs in the human body is the liver. Since the human liver has so many different activities, it is appropriately referred to as the body's metabolic factory. Its functional heterogeneity is unparalleled and interesting. In light of this, liver illness becomes a major cause for concern for people, since it is one of the most physically, emotionally, and financially exhausting diseases. Acute or chronic liver disease are both possible. Different liver diseases have different death and morbidity rates. There are numerous causes of chronic liver disease.[1]

Liver cirrhosis is defined as diffuse hepatic process characterized by fibrosis and conversion of normal liver architecture into structurally abnormal nodule.[2] It is the final common pathway for all chronic liver diseases. Cirrhosis currently causes 1.16 million deaths making it the 11th most common cause of death.[3,4] It is a major cause of morbidity and mortality in adults globally. Systemic inflammation has now been proposed to play a crucial role in the natural history of progressive liver damage. Cirrhosis associated immune dysfunction syndrome (CAID) is an entity characterised by combination of systemic inflammation and immune deficiency state. It has been described as a multifactorial process which may be secondary to an infectious or non-infectious stimulus.[5,6] The systemic inflammation has been attributed with worsening of liver failure and poor outcome. Dysfunction of innate and adaptive immune system leading to increase in pro inflammatory cytokines is responsible for local as well as systemic injury in patients with cirrhosis.[7,8]

There is an overwhelming evidence of role of inflammatory markers in pathogenesis of liver disease. So, a number of surrogate serum markers have been studied as a prognostic guide for predicting outcome and improving management of decompensated liver disease. Neutrophil to lymphocyte ratio is one such cost effective, readily available and easily calculated marker of systemic inflammation. Neutrophil count helps in identifying ongoing inflammation and lymphocyte count represents immune regulatory pathway.[9] Studies have shown NLR to be useful in predicting outcome and mortality in patients with viral hepatitis, hepatocellular carcinoma, liver transplantation and nonalcoholic fatty liver disease.[10,11,12,13]

Various studies have shown NLR as an important biomarker of ongoing inflammation and can reflect a person’s immunity to liver cirrhosis.13 In developing countries where resources are deficient, NLR is an ideal test for early detection of infection and inflammation. Recently, NLR has also emerged as a predictor of

mortality independent of MELD scores in patients with cirrhosis and with hepatocellular carcinoma, as well as in candidates on the liver transplantation list.[14,15]

Hence the present study is taken up to evaluate the role of NLR as prognostic marker in the stable cirrhotic patients.

Study Objectives: To evaluate the Correlation of NLR with Liver function in liver cirrhosis patients.

Study design: ross sectional study

Study setting: General Medicine department of the Chettinad Health and Research Institute

Study period: 2 months i.e December 2022 and January 2023

Sample size: After getting approval from the institutional ethics committee, 100 patients attending the OPD of the general medicine were included following convenience sampling.

Inclusion criteria

1. Patients (Both genders) diagnosed as Liver cirrhosis
2. Age above 18 years

Exclusion Criteria:

1. Presence of secondary immune deficiency states-HIV
2. Hepatocellular cancer patients
3. Patients on corticosteroid drugs or cytotoxic drugs
4. Patients with ongoing infection
5. Pregnancy and lactation
6. Patients not capable of giving consent (Psychiatric patients)
7. Patients not willing to participate in the study (who refused to consent)

Procedure of data collection

After getting approval from the institutional ethics committee, patients attending the General Medicine outpatient department, who are known causes of cirrhosis of liver in spite of etiology, who fulfill the inclusion and exclusion criteria are involved in the study after obtaining informed consent from the patients.

Blood samples from the patients are taken and sent for investigations. The investigations include, complete blood count and after that Neutrophil to Lymphocyte Ratio was calculated.

Patients who got admitted where thoroughly evaluated with investigations that includes,

- Complete Blood Count
- Liver Function Tests
- Serum Proteins
- Renal Function tests
- Coagulation Profile

Among these patients, those who developed complications were identified and the correlation with the already calculated Neutrophil to Lymphocyte Ratio was done and the results were analyzed. The severity of the liver disease is evaluated by Child Turcotte-Pugh score. The scoring ranges from 5 - 15 points and the patients were categorised into three groups -class: A (5 - 6), B (7 - 9), and C (10 - 15).

	Points		
Clinical and Lab Criteria	1	2	3
Encephalopathy	None	Mild to moderate	Severe
Ascites	None	Mild to moderate	Severe
S. bilirubin (mg/dL)	< 2	2 - 3	>3
S. albumin (gm/dL)	> 3.5	2.8 - 3.5	< 2.8
Prothrombin time	< 4	4 - 6	>6
Seconds prolonged INR	<1.7	1.7-2.3	>2.3

Child-Turcotte-Pugh class obtained by adding score for each parameter (total points) Class A = 5 to 6 points

(least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)

Statistical Analysis

Continuous data will be expressed as means and standard deviation. Tests of significance used are Chi square test and one-way ANOVA test. Statistical analysis will be done by using SPSS version 26. Level of significance is taken as $p<0.05$.

Results

The cross-sectional study was conducted in 100 patients attending the OPD of the general medicine.

Among them 73 were males and 27 were females. (Figure 1)

Figure 2 showed that out of 100 patients, 14% patients belong to 20- 39 years of age, 57% belong to 40-59 years of age and 29% belong to ≥60 years of age.

As shown in the table 1, Child pugh scoring was done to evaluate the severity of the cirrhosis. Among the study population 57% belong to least severe liver disease, followed by 27% belonged to moderately severe liver disease and 16% belong to most severe liver disease.

The patients were divided into three groups based on NLR: patients having NLR < 3, 3 ≥ NLR ≤ 6, and NLR > 6(Table 2). The mean age of the patients in group NLR < 3 was 39.3±3.54 years (n = 12), in group 3 ≥ NLR ≤6 was 45.3±4.54years (n = 64) and in group NLR > 6 was 63.5±6.75 years (n = 24).

The laboratory parameters (mean ± SD) were tabulated into three groups according to the NLR score and correlation analysis was done. Significant correlations were observed between NLR scores and age, platlet count, prothrombin time, INR, Total bilurubin, serum albumin and CPS scores.

Mean platlet count in study population among the NLR < 3 group was 132.34±9.54, in the 3≥ NLR ≤6 group was 127.53±9.69 and in the NLR > 6 group was 113.35 ± 10.42. Prothrombin time in patients in NLR < 3 group was 12.4±8.10, in the 3≥ NLR ≤6 group was 15.3±7.23 and in the NLR > 6 group was 19.5 ± 7.12.

Mean INR were 1.34±0.29, 1.94±0.53 and 2.61±0.44 for NLR < 3, 3 ≥ NLR ≤ 6 and NLR > 6 respectively. Mean serum bilirubin of the patients in the NLR < 3 group was 1.24±0.25, in the 3 ≥ NLR ≤ 6 group was 2.31±0.47 and in the NLR > 6 group was 3.24±0.53. Mean serum albumin of the patients in the NLR < 3 group was 3.73±0.31, in the 3≥ NLR ≤6 group was 3.13±0.33 and in the NLR > 6 group was 2.81±0.47.

CPS scores were compared and the mean CPS scores in the patients in the NLR < 3 group was 5.91±0.62, in the 3≥ NLR ≤6 group was 8.76±1.09 and in the NLR > 6 group was 12.54±0.83. These differences in the means were statistically significant.

Figure 1: Gender distribution of the study population

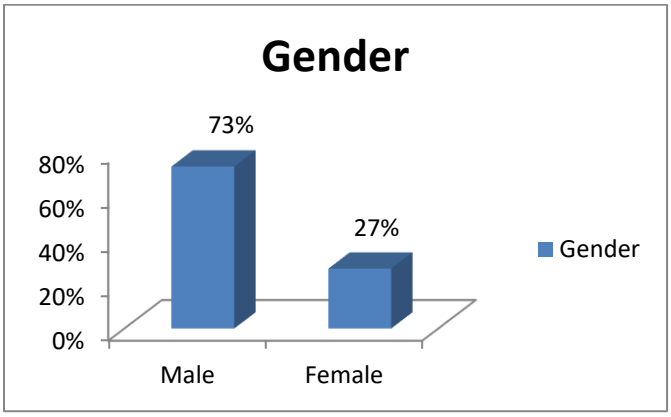

Figure 2: Age distribution of the study population

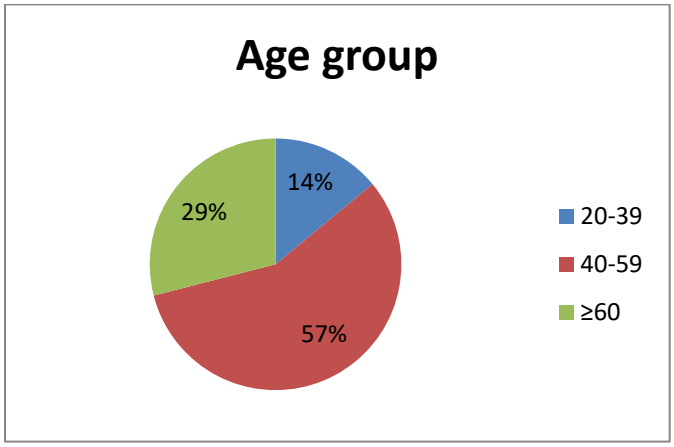

Table 1: Severity of the cirrhosis among the study population

Child pugh score	Frequency	Percentage
Least severe liver disease	57	57
Moderately severe liver disease	27	27
Most severe liver disease	16	16

Table 2: Correlation of the parameters and NLR

	NLR			
Parameter	NLR < 3 (n=12)	3 ≥ NLR ≤ 6 (n=64)	NLR > 6 (n=24)	P value
Age , years	39.3±3.54	45.3±4.54	63.5±6.75	0.0001
Male/Female	9/3	50/16	14/8	0.5332*
Haemoglobin (g/dL)	10.32±3.4	9.47±3.5	7.93±4.1	0.116
Platelet count (x109/dL)	132.34±9.54	127.53±9.69	113.35 ± 10.42	0.0001
Prothrombin time (Secs)	12.4±8.10	15.3±7.23	19.5 ± 7.12	0.014
INR	1.34±0.29	1.94±0.53	2.61±0.44	0.0001
Total bilirubin (mg/dL)	1.24±0.25	2.31±0.47	3.24±0.53	0.0001
Urea (mg/dL)	23.2±8.42	25.3± 7.89	29.1 ± 9.21	0.080
Creatinine (mg/dL)	0.81± 1.51	0.82±1.47	1.2 ± 1.53	0.551
Albumin (g/dL)	3.73±0.31	3.13±0.33	2.81±0.47	0.0001
CPS	5.91±0.62	8.76±1.09	12.54±0.83	**0.0001**

*Represents the p value calculated using chi square test

Other parameters were calculated using one way ANOVA test.

Discussion

In the present cross-sectional study, we tried to find the correlation between NLR with Liver function in liver cirrhosis patients. It was observed that NLR had a significant correlation with Child- Pugh score. s. It provides evidence that a patient with high NLR value tends to have higher CTP score. CTP score consists of five indicators which also relates to prognosis of liver cirrhotic patients.[16,17]

NLR reflects systemic inflammation as well as immune dysregulation and has previously been shown to predict prognosis in stable patients (i.e., without acute decompensation) with end-stage cirrhosis listed for liver transplantation (LT). It has been postulated that this prognostic ability of NLR reflects multiple pathways of the pathophysiology underlying chronic liver disease including induction of low-dose endotoxinemia, which in turn results in a deleterious systemic inflammatory response in cirrhotic patients.[18] As a consequence of such systemic inflammation, the intestinal barrier in cirrhotic patients is compromised. In addition, there may be a qualitative functional defect of neutrophils in cirrhotic patients – beyond their mere ratio to lymphocytes contributing to poor outcomes such as infection, organ failure and mortality.[19]

In the study conducted by He et al. NLR was significantly higher in decompensated than in compensated cirrhosis patients.[20] It was explained that in the state of decompensated cirrhosis there is a complex relationship between the systemic inflammation process and immune system.[21] In cases of compensated cirrhosis, the ligand released from damaged hepatocytes, mentioned as damaged-associated molecular patterns (DAMP) are recognised by the immune system. This

results in a sterile systemic inflammation whereas in case of decompensated liver cirrhosis, ligands produced from bacterial components are transported from intestinal tracts into the circulation via static portal circulation and fragility of the gut wall.[22] Sharma K et al. in his study demonstra ed a strong correlation between NLR and CAD (Coronary Artery Disease).[23] H.Shimada et al. in his study showed that in patients of gastric cancer with raised NLR has worst prognosis than those with low NLR.[24] Most studies have shown a higher NLR is associated with poor outcome and prognosis. However, there is no consensus for a definitive cut off value for NLR. NLR has been demonstrated as an independent marker in predicting mortality in patients with cirrhosis. In a study conducted by Jung Hyun Kwon et al. it was demonstrated that NLR was a useful predictor of mortality of 1-month survival, particularly in Child Pugh class C patients independently.[25]

In a study conducted by Vineeth V.K et al. he showed that patients with high NLR had a positive correlation with complications, thereby was associated with higher short term mortality.[26]

Conclusion

It was concluded from the study that the NLR and CPS scores are significantly correlated. The laboratory parameters (mean ± SD) were tabulated into three groups according to the NLR score and correlation analysis was done. Significant correlations were observed between NLR scores and age, platlet count, prothrombin time, INR, Total bilurubin and serum albumin.

Limitations

It was conducted for a short span of time and therefore adequate sample size could not be collected. Also, as it is a cross-sectional study, follow up of the patients could not be done. In our study, NLR was calculated only one time at admission. Serial monitoring of NLR would be necessary to diagnose complications during hospital stay.

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