



## Hematological Profile in Patients of Chronic Liver Disease Correlation of Neutrophil to Lymphocyte Ratio with Child Pugh Classes

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### ABSTRACT

A retrospective study to find the various hematological trends in patients with chronic liver disease and to investigate the correlation of neutrophil to lymphocyte ratio with the Child Pugh Scores, in order to determine a link between disease severity and prognosis.

Keywords: chronic liver disease, hepatitis, alcohol, ascites, encephalopathy, anemia, thrombocytopenia, PT, INR, Child Pugh scores, neutrophil: lymphocyte ratio, severity, correlation

### I. INTRODUCTION:

Chronic Liver Disease (CLD) is the continuous and progressive worsening of liver functions for more than 6 months. There is incessant destruction, inflammation and regeneration of the liver parenchyma that ultimately causes the liver to undergo fibrosis and cirrhosis.<sup>[1]</sup> Liver plays a major role in synthesizing clotting factors and inhibitors, erythropoiesis, detoxification; and storage of essential minerals and vitamins like iron, vitamin B12 and folic acid. Therefore, CLD causes disruption in normal homeostasis, coagulation and hematopoiesis.

As per the World Health Organization, liver disease is the tenth most common cause of death in India and CLD is the 4<sup>th</sup> most common cause of death worldwide.<sup>[2]</sup>

There are many causes of CLD.<sup>[3]</sup> Some of which are as follows:

- Chronic Viral Hepatitis: most commonly due to Hepatitis B, C and D viruses. Chronic viral hepatitis if left untreated could lead to hepatocellular carcinoma
- Alcohol
- Autoimmune Causes: Autoimmune Hepatitis, Primary Sclerosing Cholangitis, Primary Biliary Cirrhosis
- Genetic Causes: Wilson Disease, Alpha-1 Antitrypsin Deficiency, Hereditary Hemochromatosis
- Drug Induced Hepatitis: methotrexate, amiodarone, phenytoin, isoniazid
- Vascular: Budd Chiari Syndrome
- Idiopathic
- Cryptogenic

The Child Pugh Score was invented to predict the mortality in patients with CLD.<sup>[4]</sup> It includes 5 parameters as shown in Tables 1 and 2.

Table 1

Factor	1 point	2 points	3 points
Total Bilirubin (mg/dl)	<2	2-3	>3
Serum Albumin (mg/dl)	>3.5	2.8-3.5	<2.8
Prothrombin Time (PT) prolonged by (s)*	<4.0	4.0-6.0	>6



INR*	<1.7	1.7-2.2	>2.2
Ascites	None	Mild (or suppressed with medication)	Moderate to Severe (or refractory)
Encephalopathy	None	Grade I-II	Grade III-IV

\*Either the PT prolongation time or INR is used, not both.

Table 2

	Class A	Class B	Class C
Total Points	5-6	7-9	10-15
Disease Severity	Mild/ Well Compensated Disease	Moderate/ Functional Compromise	Severe/ Decompensated Disease
1 year survival rate	100%	80%	45%

The grades for Hepatic Encephalopathy<sup>[5]</sup> were defined according to the guidelines set by the American Association for the Study of Liver Diseases (AASLD), which are shown in Table 3.

Table 3

Grade	Findings
0/None	No abnormalities detected
I	Mild confusion, altered sleep rhythm, behavioral alterations
II	Asterixis, lethargy, disorientation to time
III	Gross disorientation, somnolent but responsive to stimuli, confused
IV	Coma

The neutrophil: lymphocyte ratio (N: L ratio) reflects the balance between systemic inflammation and immunity and is considered a prognostic value in cardiovascular diseases, infections, inflammatory diseases and in many types of cancers.<sup>[6]</sup> The normal range of N: L ratio in a healthy individual lies within 0.78- 3.53 (~1-3).<sup>[7]</sup> A value >6 indicates mild stress whereas a value of >9 may highlight critical illness.<sup>[8]</sup>

## II. METHODOLOGY:

This is a retrospective study conducted on a sample size of 50 patients diagnosed with Chronic Liver Disease at the Era Medical College and Hospital, Lucknow, India. Both compensated and decompensated



patients were included in the study. The patient records were accessed via the hospital’s HIS data system. The records used for this study included the age and sex of the patients, the complete blood count (hemoglobin, total leucocyte count with differential, platelet count, RBC, Hct, MCV, MCH, MCHC) total bilirubin levels, prothrombin time (PT), international normalized ratio (INR), serum albumin levels and the presence and level of clinical findings like ascites and hepatic encephalopathy.<sup>[9, 10, 11]</sup>

The Neutrophil to Lymphocyte Ratio (N: L Ratio) and the Child Pugh Scores were then calculated from the values observed in the parameters mentioned above.<sup>[12]</sup>

The inclusion criteria included patients that had been admitted on or after January 1, 2022 and the hematologic profiles included in the study were the very first tests being done on them; thus, making sure that no effect of treatment given to them during their course of hospital stay was reflected in the values noted.

Patients with a primary coagulation disorder, a known gastrointestinal malignancy or hepatocellular carcinoma, an acute infection or sepsis and those with acute liver failure were excluded from this study.

As this is a total retrospective study using the hospital’s digital database, no breach of ethics took place and identity of patients was not disclosed.

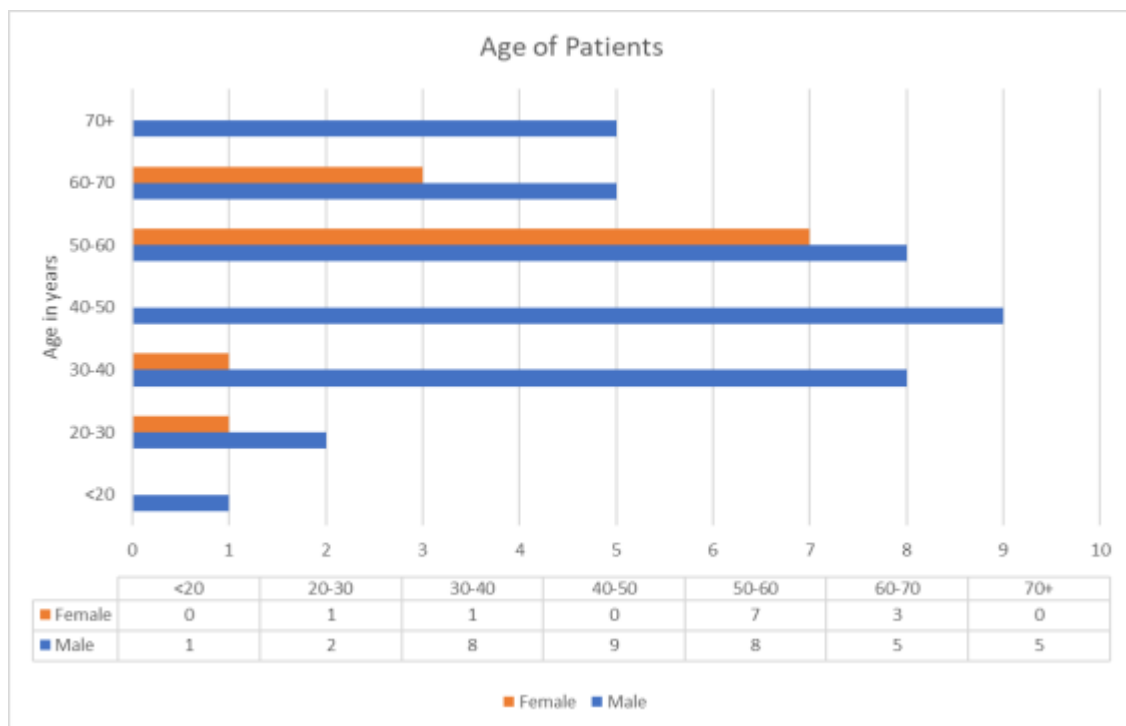
### III. RESULTS:

The mean age observed among these patients was 51.5 years (SD= 14.515), with the youngest patient being 15 years of age and the oldest patient being 80 years of age(Figure 1).<sup>[13]</sup>

38 out of the 50 patients studied were males (76%) and the remaining were females, 12 (24%).

The causes of chronic liver disease seen in these patients ranged from idiopathic, 21 (42%), viral, 19 (38%), alcohol, 5 (10%), non-alcoholic fatty liver disease (NAFLD), 2 (4%), to 1 each of cryptogenic, disseminated tuberculosis and drug induced chronic liver disease (2%)(Figure 2).<sup>[14, 15]</sup>

Figure 1



26 patients (52%) presented with a low hemoglobin level of less than 10mg/dl. 32 patients (64%) had decreased red blood cell (RBC) values and the most common anemia observed was normocytic normochromic anemia, in 39 patients (78%),

followed by microcytic anemia, 7 (14%) and macrocytic anemia, 4 (8%). All findings of macrocytic anemia were observed in patients whose cause of chronic liver disease was found to be alcohol (100%)(Figure 3).<sup>[16, 17]</sup>

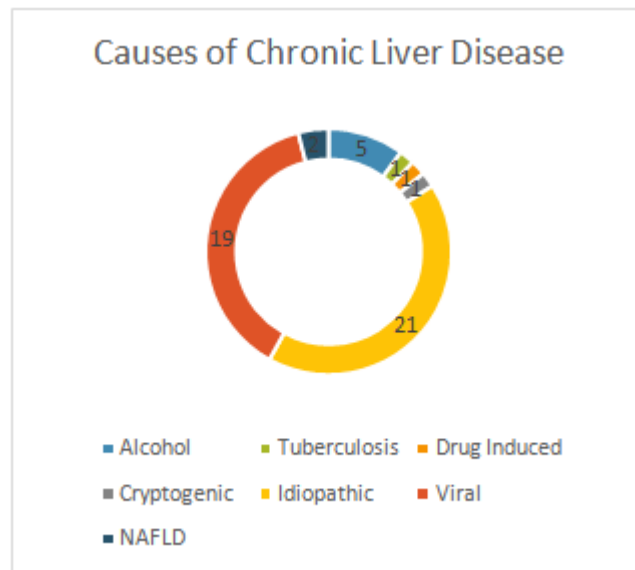


Figure 2

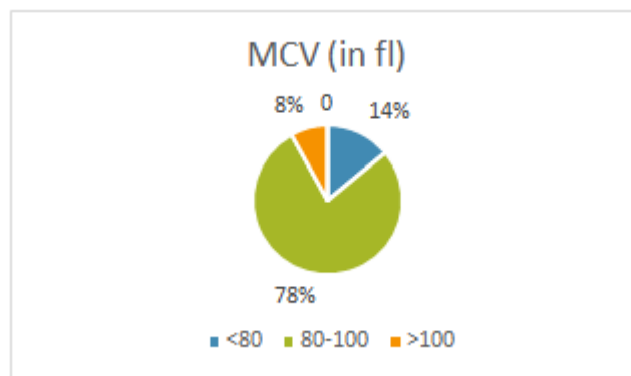


Figure 3

39 patients (78%) had thrombocytopenia on arrival,<sup>[18]</sup> 38 of them (76%) had a prolonged prothrombin time (PT) and 43 patients (86%) had a higher INR than 1.1. The prolonged PT and INR values suggest the deficiency of clotting factors that are normally synthesized by the liver.<sup>[19]</sup>

11 patients (22%) had an increased total leukocytes count (TLC), with 27 (54%) presenting with high neutrophil cell counts. No patient was found to have neutropenia. Lymphopenia was seen in 30 patients (60%).

A neutrophil: lymphocyte ratio (N: L ratio) in the normal range of roughly 1-3 was seen in 13 individuals (26%). However, a N: L ratio between 6-9 and a ratio above 9 were seen in 3 patients (6%) and 12 patients (24%) respectively.

41 patients (82%) had mild amount of ascites present which was well managed by medications, whereas 5 (10%) presented with no

ascites on admission. The remaining 4 (8%) patients had moderate to severe ascites.

Only 2 patients (4%) presented with severe encephalopathy (grade III-IV). 44 patients (88%) had hypoalbuminemia, out of which 21 (47%) had their serum albumin in the range of 2.8-3.5mg/dl and 23 (53%) had serum albumin levels below 2.8mg/dl.<sup>[20]</sup>

Normal total serum bilirubin values were noted in 21 admissions (42%) whereas 29 (58%) had values above the upper limit of 1.2mg/dl.

Child Pugh Classes were calculated based on the Child Pugh criteria and the results were the following: Class A (4%), Class B (62%), Class C (34%)(Figure 4). Out of the 12 patients who had a N: L ratio of more than 9, 7 were found to have a Child Pugh Class C classification (58.33%). This directly correlated with disease severity. The findings of encephalopathy and ascites were also found to be more severe in these patients.<sup>[21, 22]</sup>

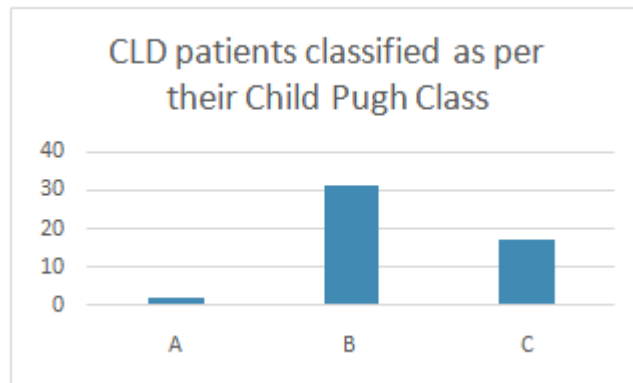


Figure 4

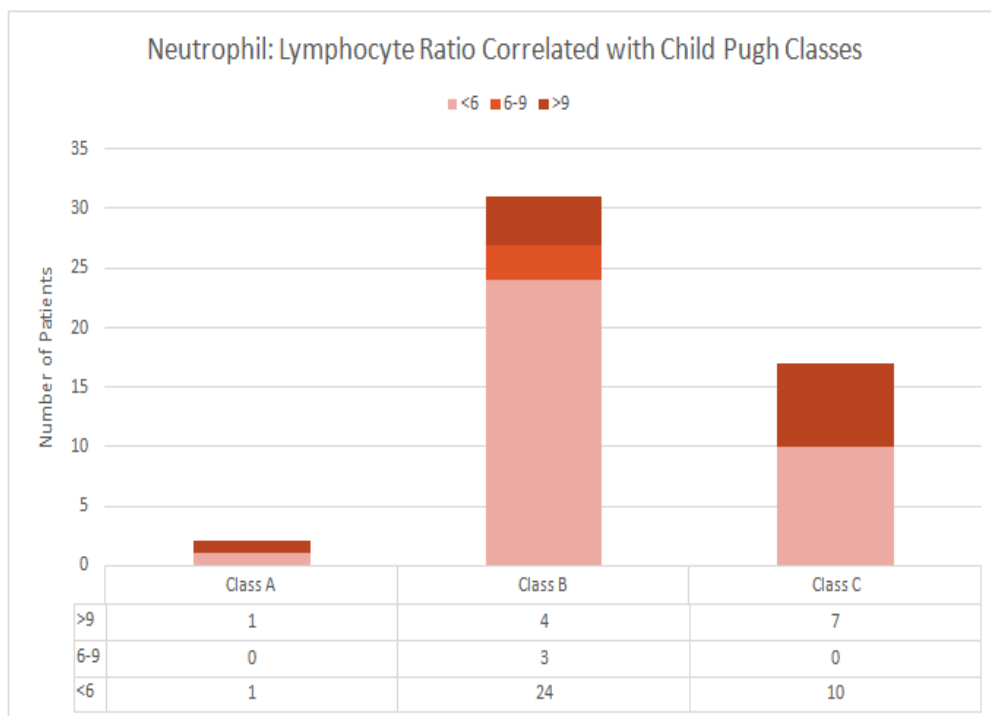


Figure 5

#### IV. CONCLUSION:

The most common hematological abnormalities seen were thrombopenia, prolonged PT and INR, and normochromic and normocytic anemia.

Ascites was present in 90% of the study sample with 8% having severe refractory ascites that did not respond well to medical treatment.

Also as observed in the data mentioned above, the N: L ratio value of >9 seen in 12 patients had a 58.33% chance to be classified as Child Pugh Class C. That means out of these 12 patients, 7 belonging to class C and with a N: L ratio of greater than 9 had severe decompensated chronic liver disease that had a poor prognostic value(Figure 5).

This concludes our study.

#### Declaration of conflicting interests:

The authors declare no conflict of interest in preparing this paper.

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