



## Pattern of Hematological Abnormalities in Chronic Liver Disease

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### Abstract

**Background:** Chronic Liver Disease (CLD) is an end stage parenchymal liver disorder and is commonly associated with hematological abnormalities. The aim of this study was to evaluate the patterns of hematological abnormalities in patients of CLD

**Material and methods:** The study was conducted in department of Pathology, ASCOMS and Hospital over a period of one year and included 68 patients of CLD. Patients were evaluated for hematologic indices.

**Results:** Among the 68 patients in our study, male preponderance was observed with majority of patients in age group of 41-70 years. Anemia was observed in 97% of cases with 50% showing severe anemia. Leukocytosis was observed in 38.23% cases and thrombocytopenia in 55.88% cases. Prothrombin time was prolonged in 27.9% of patients.

**Conclusion:** This study inferred that CLD is frequently associated with hematological alterations. Early identification and correction of hematological abnormalities in CLD patients can effectively reduce mortality and morbidity.

**Keywords:** Chronic Liver Disease (CLD), Hematological Abnormalities, Anemia

### INTRODUCTION

Chronic Liver Disease (CLD) is an end stage disease with progressive deterioration of liver functions for more than six months. It is the 4<sup>th</sup> most common cause of death in adults worldwide [1]. CLD is frequently associated with one or the other hematological abnormality and the severity of hematological abnormalities increases as the disease progresses [2]. Liver plays a key role in synthesis of clotting factors, protein biosynthesis, lipid metabolism and detoxification of harmful metabolic products. Various causative factors for CLD are viral infections, alcohol abuse for a prolonged time, nonalcoholic fatty liver disease or nonalcoholic steatohepatitis, toxins, autoimmune diseases, genetic and metabolic disorders [3].

CLD leads to hematological abnormalities involving both cellular and soluble blood components [4]. Multiple factors are attributed to the hematological changes which include hepatic synthetic dysfunction, portal hypertension induced sequestration, viral and toxin induced bone marrow suppression and alteration in bone marrow stimulating factors [2]. The common hematological problems encountered in CLD are anemias, cytopenias, thrombocytopenia and coagulation abnormalities resulting in increased morbidity and mortality. Hence, it is necessary to identify these hematological alterations for early correction to decrease adverse events.

The present study was undertaken to evaluate and analyse hematologic indices of CLD patients so that

they can be therapeutically managed for these complications earlier and consequently reduce morbidity and mortality.

### Material and Methods

The study was conducted in the Post Graduate Department of Pathology, ASCOMS and Hospital, Jammu after obtaining ethical clearance from the Ethics Committee of ASCOMS & Hospital. This study was conducted over a period of one year from 1<sup>st</sup> November 2019 to 31<sup>st</sup> October 2020.

Patients of Chronic Liver Disease were studied based on the inclusion and exclusion criteria after the informed consent given by the patient.

### INCLUSION CRITERIA:

Patients with documented CLD i.e. patients with liver disease whose symptoms and signs persist for more than 6 months

### EXCLUSION CRITERIA:

- a) Patients with underlying malignancy or known primary Hepatocellular carcinoma.
- b) Patients with primary coagulation disorder and primary abnormalities of hemostatic function.
- c) Acute Hepatic Failure.
- d) Patients with preexisting anemia due to other causes.
- e) Patients suffering from end stage diseases like Coronary Artery Disease, Cardiac Failure, Chronic Kidney disease.

The patient's detailed history and clinical details were recorded. Results of investigations viz LFTs (Liver Function Tests), serological tests for viruses, radiology were recorded. The investigations performed on each patient included complete blood counts, peripheral smear examination, coagulation profile [5].

### Results

Sixty-eight patients with chronic liver disease were included in this study. There were 53 males (77.94%) and 15 females (22.06%). The age of the patients ranged from 25 to 75 years, with the mean age being  $55.97 \pm 12.05$  years. Majority of the cases belonged to the age group 41- 70 years (80.88%) with a peak in the 7<sup>th</sup> decade (32.35%). Table 1 and Table 2 depicts the

gender and age wise distribution of patients, respectively.

Majority of the patients (54.41%) in the study were labelled as Alcoholic Liver Disease (ALD) followed by Non-alcoholic Steatohepatitis (NASH) in 26.47%, Hepatitis B in 10.3% and Hepatitis C in 5.89% patients. Etiology remained undetermined in 2 patients (2.94%).

### Hematological changes:

Hemoglobin ranged from 2.1 g/dl to 14.8 g/dl, with the mean hemoglobin of 8g/dl. Most of the patients 66 (97%) were anemic, with predominance of severe degree in (50%), followed by moderate grade in (34.84%) and mild degree in (15.15%) patients. Only 2 patients (3%) had normal hemoglobin levels. Lowest hemoglobin value observed was 2.1g/dl in a patient of cirrhosis with unknown etiology who had Grade III esophageal varices and had multiple episodes of hematemesis and blood in stools.

Among the 66 anemic patients, normocytic red cells were noted in maximum (51.51%) followed by macrocytic (33.33%) and microcytic (15.15%) red cell morphology on PBF, depicted in Fig.1. Macrocytic red cells were mostly seen in patients of Alcoholic Liver Disease, 20 out of 35 patients (57.14%) with macrocytosis. The predominant poikilocytes seen on the peripheral smear were the Target cells. Other poikilocytes like burr cells and tear drops cells were seen occasionally corresponding to the severity of anemia.

The analysis of WBC's was done with the total count and the differential count. The total count of WBC ranged from 1700/mm<sup>3</sup> to 36,800/mm<sup>3</sup>. Among the 68 patients studied, leukocytosis (TLC>11,000/cumm) was observed in 26 patients (38.23%). Leucopenia (TLC<4000) was observed in 5 patients (7.35%).

Thrombocytopenia was observed only in 38 patients (55.88%). Out of these 38 patients, 21(31%) had moderate thrombocytopenia, 16(24%) had mild thrombocytopenia while severe thrombocytopenia was observed only in 1 case (Table 3). Moderate to severe thrombocytopenia was found in patients with moderate to massive splenomegaly and had history of various episodes of hematemesis. 40 patients (58.82%) had splenomegaly, out of which 21 patients had thrombocytopenia. 41 patients (60.29%) had

esophageal varices, out of which 27 patients had thrombocytopenia.

Among 68 patients, 19 (27.9%) had prolonged prothrombin time (>16 seconds) and 49 (72.06%) had normal prothrombin time (13- 16seconds). Majority of the patients (39.7%) with prolonged PT had history of at least one episode of hematemesis (Fig 2).

**Table 1: Sex Distribution of 68 CLD Patients**

| Gender | No. of Cases | Percentage (%) |
|--------|--------------|----------------|
| Male   | 53           | 77.94          |
| Female | 15           | 22.06          |
| Total  | 68           | 100            |

**Table 2: Age distribution of CLD Patients**

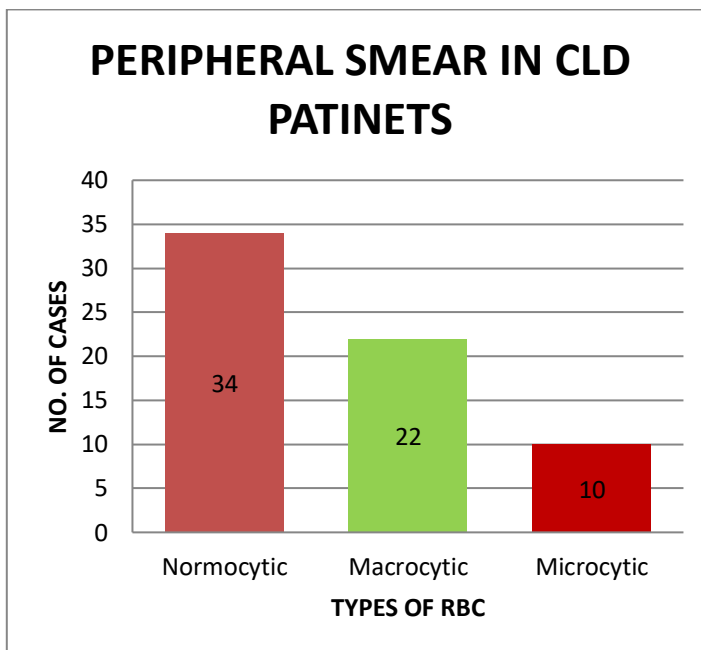
| Age (years) | No. of cases | Percentage (%) |
|-------------|--------------|----------------|
| 21-30       | 2            | 2.94           |
| 31-40       | 6            | 8.82           |
| 41-50       | 16           | 23.53          |
| 51-60       | 17           | 25             |
| 61-70       | 22           | 32.35          |
| 71-80       | 5            | 7.35           |
| Total       | 68           | 100            |

**Table 3: Distribution of Cases According to Platelet Count**

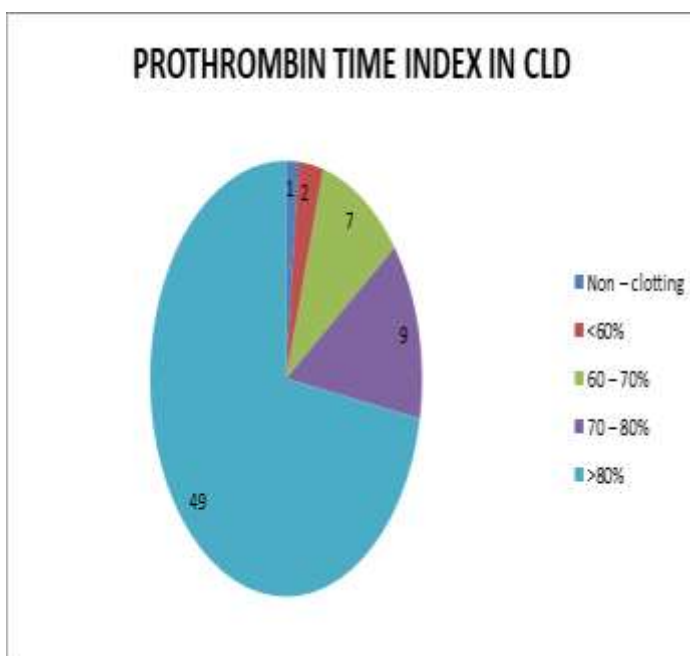
| Platelet Count                                 | No. of cases | Percentage (%) |
|--|--------------|----------------|
| Normal Count                                   | 30           | 44             |
| Mild Thrombocytopenia (<1.5 lac/cumm)          | 16           | 24             |
| Moderate Thrombocytopenia (50,000- 1 lac/cumm) | 21           | 31             |

|  |    |     |
|--|----|-----|
| Severe Thrombocytopenia (<50,000/cumm) | 1  | 1   |
| <b>Total</b>                           | 68 | 100 |

**Figure 1: Types of Anemia in CLD Patients**



**Figure 2: Prothrombin Time Index in CLD Patients**



**Discussion**

Chronic liver disease is a progressive end stage liver disease. Abnormalities in hematological indices are frequently observed in CLD. The present study included 68 patients of CLD. The mean age was falling in the 6<sup>th</sup> decade which is similar to the studies done by Kaur *et al* and Selvamani S *et al*[6,7]. This study agrees with most of the other studies in terms of increased male preponderance, which is attributed to the high prevalence of risk factors for CLD in males [6,7,8].

Alcoholism was the leading cause of CLD among the study group with alcoholic liver disease (ALD) constituting 54.4% as native chronic liver disease followed by NASH, Hepatitis B, Hepatitis C and undetermined which is in agreement with studies by Kaur J *et al*, Selvamani S *et al* and Solomon RT *et al*[6,7,8]. The difference in the distribution of etiology in the study by Ozatli D *et al* is attributed to the racial, geographical and lifestyle distribution in various study groups [9].

CLD is associated with anemia in majority of the patients. The mean Hemoglobin in the present study is 8.05g/dl. The results of our study were in concordance with Selvamani S *et al*, Chauhan N *et al*, Khare S *et al*[7,10,11]. Approximately 75% of patients with CLD develop anemia. The blood volume in liver disease averages 10 to 15% greater than normal resulting in hemodilution which tends to exaggerate the prevalence and degree of anemia[12]. The major causes of anemias are gastrointestinal hemorrhage and hypersplenism secondary to portal hypertension. The anemia is usually mild to moderate in the absence of any complicating factors such as marrow suppression by exogenous agents or nutritional deficiency. The hemoglobin level rarely falls below 10g/dl in the absence of bleeding or severe hemolysis. Alcohol abusers can develop anemia due to folate deficiency or direct suppression of hematopoiesis by alcohol [13]. Patients with cirrhosis due to any etiology are at increased risk of hemorrhage. Blood loss is seen in 24 to 70% patients of alcoholic cirrhosis [14].

In the present study, normocytic normochromic anemia was the predominant finding in the peripheral smear in the majority of cases (52.9%) which was similar to that reported by Jha SC *et al*, Kaur J *et al* and Selvamani S *et al* in their study [1,6,7]. Macrocytic anemia was seen in 22 cases in the present study. Majority of the cases belonged to ALD category.

Macrocytosis in cirrhosis can be due to effects of alcohol on RBC production in the bone marrow and vitamin B12 and folic acid deficiency [1,15]. Microcytic anemia was seen in 10 cases in the present study, and all the 10 patients had bleeding esophageal varices, 8 out of 10 patients had splenomegaly. Esophageal varices and portal hypertensive gastropathy may be associated with chronic loss of blood into the gut and development of chronic iron deficiency anemia [16].

Mean WBC count is within normal range in the present study (10.85 mm<sup>3</sup>) which is slightly high compared to other studies done by Ozatli *et al*, Ansari MZ *et al*, Goulis J *et al*[9,17,18]. Significant number of cases (38.23%) had leukocytosis which was mostly due to infections due to community acquired infection, nosocomial infections, spontaneous bacterial peritonitis and secondary peritonitis due to repeated paracentesis. Leucopenia was observed in 7.35% patients. The causes of leucopenia in CLD are portal hypertension induced sequestration, alterations in granulocyte colony stimulating factor and granulocyte macrophage-colony stimulating factor and bone marrow suppression mediated by toxins [19].

The mean platelet count in CLD in the present study is 1.42 lac/mm<sup>3</sup> which is similar to the study done by Ozatli *et al*[9]. Studies done by Ansari MZ *et al*, Goulis J *et al* and Lv Y *et al* show relatively low platelet counts [17,18,20]. Thrombocytopenia was observed in 38 out of 68 patients of CLD and normal platelet counts in 30 patients (44%). Amongst thrombocytopenic patients, 42% had mild thrombocytopenia (<1.5 lac/mm<sup>3</sup>), 55.2% had moderate thrombocytopenia (1-1.5 lac/mm<sup>3</sup>) and 2.6% had severe thrombocytopenia (<50,000/mm<sup>3</sup>). This conforms to the study by Kujovich JL[21]. Multiple factors contribute to the development of thrombocytopenia and these can be broadly divided into those that cause bone marrow suppression, hypersplenism and increased destruction. Thrombopoietin levels are decreased in CLD resulting in thrombocytopenia [3]. Decreased platelet production can also be due to bone marrow suppression by viruses, alcohol, iron overload and medications. The increased platelet destruction in cirrhotic patients also occurs because of increased shear stress, fibrinolysis and bacterial infections.

In our study increased prothrombin time was found in 19 patients (27.9%), out of which 14 patients had upper GI bleed. Study done by Solomon RT et al reported 72% patients with elevated prothrombin time and study done by Selvamani S et al reported 46% patients with prolonged prothrombin time[7,8]. Prothrombin time (PT) is a measure of synthetic functions of liver and is involved in most of the liver diseases as coagulation factor synthesis is impaired in CLD [3]. Gastrointestinal hemorrhage is one of the most common complications in advanced liver disease patients with deranged coagulation indices. In our study, 39.7 % patients with prolonged PT had history of at least one episode of hematemesis. Hemostatic defects in liver disease patients can be due to several reasons which include thrombocytopenia, alterations in platelet and endothelial cell function, fibrinolysis and renal failure. In chronic liver disease (CLD), prolongation of PT is not seen initially until the stage of cirrhosis and the liver fibrosis is reached.

### Conclusion

From this study, it is concluded that CLD is frequently associated with hematological abnormalities. Anemia of diverse etiology occurs in many of these patients. Altered leukocyte counts can be observed. They are at an increased risk of bleeding due to thrombocytopenia and coagulation defects. Each patient's risk should be assessed in an attempt for better management of CLD patients, thereby, reducing morbidity and mortality.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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