# A STUDY OF VARIATION IN HAEMATOLOGICAL PARAMETERS IN CHRONIC LIVER DISEASE

*Meethu Rappai[1], Purnima S. Rao[2], Sandhya Ilanthodi[3]*

*[1]Postgraduate Student, Department of Pathology, A. J. Institute of Medical Sciences and Research Centre, Mangaluru, Karnataka, India.*
*[2]Associate Professor, Department of Pathology, A. J. Institute of Medical Sciences and Research Centre, Mangaluru, Karnataka, India.*
*[3]Associate Professor, Department of Pathology, A. J. Institute of Medical Sciences and Research Centre, Mangaluru, Karnataka, India.*

**ABSTRACT**

**BACKGROUND**

Chronic Liver Disease (CLD) is a disease process causing progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. It is frequently associated with haematological abnormalities and causes complications including bleeding and infection which can increase morbidity and mortality rate. Dietary deficiencies, bleeding, alcoholism and abnormalities in hepatic synthesis or proteins used for blood formation or coagulation add to the problem of liver disease. Therefore, wide range of haematological abnormalities is seen in liver disease. This study studies the correlation between abnormalities in haematological parameters and severity of chronic liver disease.

**METHODS**

100 chronic liver disease patients were studied retrospectively and prospectively for a period of one year from January 2018 to December 2018. In all cases, patients age, gender and relevant clinical history were obtained.

**RESULTS**

In chronic liver disease patients, all haematological parameters were decreased except MCV and MCH which were increased. However, it was not statistically significant. Prolonged PT and abnormal peripheral smears were also seen. A table of all haematological parameters studied by mean, interquartile range, median and standard deviation was prepared. Mann Whitney test was used to calculate p value.

**CONCLUSIONS**

Chronic liver disease patients are frequently associated with haematological and biochemical abnormalities showing anaemia, leucopenia and thrombocytopenia along with derangement in liver enzymes and decrease in renal function test. Prolonged prothrombin time and abnormal peripheral smear are also seen in these patients. It is associated with increased morbidity and mortality. In our study, haematological parameters (Hb, RBC, PCV MCHC, platelet, PT) all were decreased except MCV and MCH which were increased. However, MCH was statistically not increased. MCV was reduced significantly and biochemical parameters like deranged liver function test were all increased except total protein, albumin and renal function test. S. Urea and Creatinine were reduced. Thus, the complete blood count picture had shown the picture of anaemia, leucopenia and thrombocytopenia. Highly significant p values <0.001 were seen.

**KEY WORDS**

Chronic Liver Disease, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH)

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## BACKGROUND

Liver is one of the largest organs of the body weighing 1-1.5 Kg, which is 1.5-2.5% of the lean body mass. It performs numerous and vital roles in maintaining homeostasis and health. It plays major role in synthesis of proteins, regulation of nutrients, metabolism and conjugation of bilirubin and drugs, detoxification, production of bile and maintenance of immunity (Kupffer cells). Right from being a primary site of haematopoiesis in foetal life to maintenance of haematological parameters in postnatal life, the liver has an extremely important role in maintenance of blood- homeostasis. It stores iron, folic acid and vitamin B12, secretes clotting factors and inhibitors. Hence, liver diseases cause wide range of abnormalities in haematological parameters. Chronic Liver Disease (CLD) refers to process causing progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. Disease process involves progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. Peripheral blood picture in chronic liver disease is influenced by the presence of jaundice, liver cell failure, portal hypertension and hypersplenism, reduced red cell half-life. CLD is frequently associated with haematological abnormalities and is associated with increased morbidity and mortality in these patients.[1]

It causes generalized suppression of blood cell production and produces abnormal blood cell precursors that cannot mature into functional cells. The changes frequently seen in CBC (Complete blood count) are anaemia, structurally abnormal RBC's, reduced numbers of WBC's, and platelets. Alcohol acts as CNS depressant although some behavioural stimulation is also observed. Alcohol affects almost all organs including CNS, GIT, CVS, hematopoietic system, genitourinary system. Alcohol is a direct hepatotoxin, but only 10-20% of

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*Corresponding Author:*
*Purnima S. Rao,*
*#604, Sheshkamal Apartment,*
*Matadakani Cross, Near Barke Police Station,*
*Gandhinagar, Mangalore,*
*Karnataka, India.*
*E-mail: purnimashenoy@gmail.com*
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alcoholics develop alcoholic hepatitis. Liver function tests are altered only in the later stages of alcoholic liver disease. Heavy drinking alters some biochemical parameters like gamma-glutamyl transferase or mean corpuscular volume.[2]

The most common cause of chronic liver disease is alcoholism which causes derangement in haematological and biochemical parameters. Due to the fact, that alcohol use, especially in heavy drinkers, can cause different metabolic derangements, it is necessary, to investigate the changes of complete blood count. Chronic excessive alcohol ingestion reduces the number of blood cell precursors in the bone marrow and causes characteristic structural abnormalities in these cells, resulting in fewer-than-normal or non-functional mature blood cells. As a result, alcoholics may suffer from moderate anaemia, characterized by enlarged, structurally abnormal RBC's; mildly reduced numbers of WBC's, especially of neutrophils; and moderately to severely reduced numbers of platelets. Since liver plays key role in both protein biosynthesis and lipid metabolism any hepatic dysfunction will lead to adverse effects on both cellular and soluble components of blood.[3]

Anaemia can occur due to abnormal lipid composition of the red blood cell membrane leading to formation of acanthocytes and ultimately causing haemolysis whereas in alcoholic liver disease it is usually attributed to spur cell anaemia. The coagulopathy of liver disease is complex associated with prothrombotic state and advanced disease pancytopenia and coagulopathy associated with haemorrhage.[4] Anaemia in chronic alcoholic liver disease is associated with direct toxic effect of alcohol on the bone marrow, causing irreversible suppression of haematopoiesis and subsequently anaemia with impaired platelet production and function. Therefore anaemia in patients with liver cirrhosis is acute or chronic blood loss into gastrointestinal tract causing iron deficiency anaemia (IDA).[5]

Many studies have has shown that the most frequently seen changes in CLD are normocytic and macrocytic cells and they are related with MCV. It plays a important role in the distinctive diagnosis of anaemia. It also has high predictive value for proving liver diseases due to alcohol and chronic alcohol usage. Macrocytosis is seen high in clinical cases diagnosed as having CLD especially due to alcohol even without existence of anaemia.[6]

Another haematological abnormality seen in chronic liver disease is thrombocytopenia due to abnormality in synthesis in coagulation protein. Commonly seen in 76% of cirrhotic patients. Pathogenesis of thrombocytopenia is multifactorial and recent studies have shown that the mechanism of thrombocytopenia specific to liver disease is due to reduced thrombopoietin production by liver and an autoimmune component.[7]

Also under normal conditions, circulating platelets, whose lifespan is about ten days, exist in the resting form with a stable surface membrane structure. During tissue damage or inflammation, the platelets stick to the lesions of the blood vessels and adhere to the exposed endothelial tissues. The HCT is one of the main factors influencing platelet adherence to the vessel wall, and the elevation of the HCT causes an increase in platelet accumulation. Although research has contributed substantially to our understanding of the relation of drinking to specific disorders, the effect of alcohol consumption on health outcome is complex and multidimensional.[8]

Many studies suggest that the presence of haematological cytopenia is associated with poor prognosis in chronic liver patients having cirrhosis. It has been reported that medically diagnosed alcoholics can be differentiated from non-alcoholics using clinical laboratory tests. Moreover, distinguishing alcoholic from non-alcoholic liver disease has important implications for treatment and management. Therefore heavy alcohol intake with a significant increase of all cause and non-cardiovascular mortality rates especially by cirrhosis, cancer and violent deaths. They also reported that all-cause mortality rates are lower for moderate drinkers than for non-drinkers, because of a lower heart disease.[9]

Abnormalities in haematological parameters cause increase risk of complications including bleeding and infection which can increase morbidity and mortality rate. Dietary deficiencies, bleeding, alcoholism and abnormalities in hepatic synthesis or proteins used for blood formation or coagulation add to the problem liver disease. Hence wide range of haematological abnormalities is seen in liver disease.[10] Therefore this study correlation between abnormalities in haematological parameters with severity of chronic liver disease can be revealed and future complications can be prevented.

## METHODS

This descriptive comparative study was undertaken in tertiary care centre in coastal Karnataka. A total of 100 chronic liver disease patients were studied from January 2018 to August 2018 and was compared with 100 normal control. In all the cases age, gender and relevant clinical history were obtained. Sample size was taken based on the convenience of the study.

Patient's demographic data and history were recorded, complete physical examination was conducted, and haematological parameters were measured for all subjects in this study.

### Complete Blood Count (By Automated Counter)

- Haemoglobin in gm%.
- RBC count in million/cmm.
- Total WBC count in cells/cmm.
- MCV in fl.
- MCHC in pg.
- Platelet count in lakhs/cmm.
- Microscopic peripheral smear study.
- Prothrombin time in seconds.
- Liver function study- Total bilirubin, Direct and Indirect fraction, SGOT, SGPT, Total protein, Albumin, Alkaline phosphatase.

### Inclusion Criteria

1. Chronic liver disease patients with abnormalities in liver function test with elevated total bilirubin, direct bilirubin, serum globulin, aspartate amino transferase (AST), alanine amino transferase (ALP).
2. Age group 18-75 yrs.

### Exclusion Criteria

1. Haematological malignancies

2. Infants and children
3. Patients with pre-existing anaemia
4. Patients suffering from end stage medical disease like COPD, coronary artery disease, ca.

**Haematological Analysis**

All EDTA-anticoagulated blood samples were obtained to perform complete haemogram analysis using Automated Haematology analyser (Sysmex XN 1000) and liver and renal function test by using Architect Abbott c1 4100.

The normal range of complete hemogram parameters are Hb- 10-12 gm/dl, RBC- 4-5.5 million/cmm, PCV- 35-45%, MCV- 76-100 fl, MCH- 27-32 pg, MCHC- 32-35%, Platelet- 150-450 lakhs/cmm, Prothrombin time- 12-14/second, ESR- 0-10 mm/hr.

**Liver Function Test**

Total bilirubin- <1.2 mg/dl, Bilirubin direct- <0.4 mg/dl, Total protein- 6.2-8 gm/dl, Serum albumin- 3.4-5.5 g/dl, Serum. Globulin- 2.3-3.5 g/dl, AST- 5-46 U/L, ALP- 5-49 U/L.

**Renal Function Test**

Serum Urea- 15-45 mg/dl, Serum Creatinine- 0.7-1.4 mg/dl.

**Statistical Analysis**

All the haematological and biochemical parameters were expressed by mean and Interquartile range (IQR). A p-value was calculated by Mann Whitney test. Further test like standard deviation and median was calculated as the data was not correlating with normality. A p-value of <0.001 was considered significant.

**RESULTS**

A total of 100 chronic liver disease patients were studied who had abnormalities in liver function test with elevated total bilirubin, direct bilirubin, serum globulin, aspartate amino transferase (AST), alanine amino transferase (ALP). Total protein and albumin were decreased in these patients.

The patient's age was ranging from 18-71 yrs. with predominance of male. There was decrease in complete blood parameters (Hb%, Mean RBC count, mean MCH, MCHC and platelets), except MCV and MCH was increased. The deranged liver function test showed total protein and albumin levels lower in these and renal function parameters especially serum urea and creatinine not significantly altered.

| | Group | Mean | Std. Deviation | Mann Whitney Test p value (Medians from CLD and Control Group) | 25th Percentile | Median | 75th Percentile |
|---|---|---|---|---|---|---|---|
| HB | Chronic Liver Disease | 9.71 | 2.92 | <0.001 | 8.23 | 9.60 | 11.38 |
| RBC | | 2.95 | .69 | <0.001 | 2.44 | 2.90 | 3.54 |
| PCV | | 27.52 | 10.37 | <0.001 | 22.43 | 26.55 | 31.43 |
| MCV | | 89.62 | 11.55 | 0.141 | 84.75 | 90.85 | 95.73 |
| MCH | | 31.56 | 5.40 | 0.400 | 31.05 | 31.55 | 34.55 |
| MCHC | | 30.68 | 4.77 | <0.001 | 28.28 | 33.20 | 33.75 |
| Platelet | | 132.22 | 90.98 | <0.001 | 82.00 | 116.00 | 151.50 |
| PT | | 28.46 | 32.47 | 0.001 | 18.70 | 21.85 | 28.15 |
| S. Urea | | 35.12 | 26.51 | 0.786 | 17.00 | 28.00 | 47.00 |
| S. Creatinine | | 1.30 | .99 | 0.600 | .80 | .90 | 1.53 |
| ESR | | 44.88 | 34.09 | <0.001 | 13.50 | 39.00 | 76.50 |

***Table 1. Haematological Parameters in Chronic Liver Disease Patients***

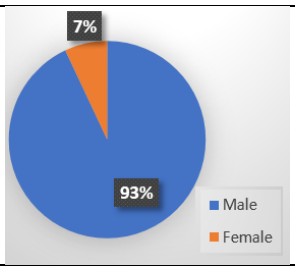


***Figure 1. Gender Distribution in Chronic Liver Disease Patients***

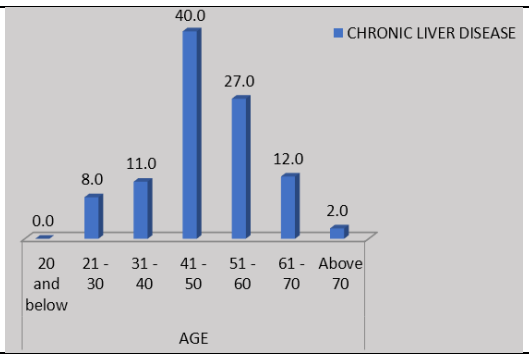


***Figure 2. Age Distribution in Chronic Liver Disease Patients***

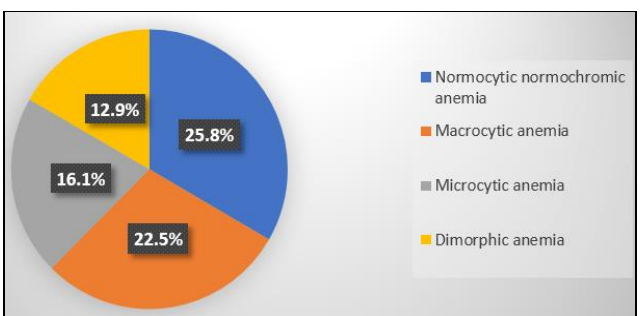


***Figure 3. Peripheral Smear Distribution in Chronic Liver Disease Patients***

**DISCUSSION**

Chronic Liver Disease (CLD) refers to disease of the liver, which last for more than six months and involves progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. The most common cause of CLD is alcoholism. [11] Alcohol abuse is a one of the most common problem encountered in India, especially among men and among young adults. Therefore, patients who have varying degrees of compensated liver function and clinicians need to differentiate between those who have stable, compensated cirrhosis and those who have decompensated cirrhosis. [12]

Various studies have shown that haematological and biochemical parameters are altered in these patients. In this study 7 patients were female, and 93 patients were male which was comparable to study done by Suresh et al in which 85% were males and 15% were females. Mean age of study

population in this study was 49.3 with 40% patients belonging to 41-50 years of age. 27% patients were more than 51 years of age and 16% less than 40 years of age. In this study 72% patients were anaemic. Mean Hb in males were lower than female. A study by Rosario Gonzalez-Casas et al showed that anaemia due to various aetiologies occur in 75% cases of CLD patients which was comparable in this study. Most of cases in this study group were alcoholics and all were men and so low mean Hb were observed in men than in females and alcoholics are at more risk of anaemia by various mechanisms and comparable results were seen in study done by Suresh et al also. Most common anaemia observed in this study was normocytic normochromic anaemia (25.8%), 22.5% had macrocytic anaemia and 16.1% had microcytic hypochromic anaemia and 12.9% dimorphic blood picture was observed. This was comparable to a study done by Suresh et al in which most common anaemia observed was normocytic normochromic (40.9%), macrocytic anaemia in 28.8%, microcytic anaemia in 22.7% and 4% in dimorphic anaemia.

In this low Hb values goes in parallel with low PCV and RBC value in most of the cases and mean PCV value is 27.5%, mean RBC count was 2.9 million/cmm which was comparable to study done by Suresh et al. Thrombocytopenia was seen in 59.8% of cases and abnormal prothrombin time was seen in 95.8% cases and was comparable with study done by Rajkumar et al. Mean corpuscular volume(MCV) and Mean corpuscular haemoglobin (MCH) were the parameters which were increased in this study which was comparable with study done by Esmeralda et al and Maruyama et al where MCV was significantly increased. Deranged liver function test was seen in which all parameters were elevated except total protein and albumin was decreased in our study which was comparable to study done by Elanchezhian et al. Renal function test were not altered.

## CONCLUSIONS

Chronic liver disease patients are frequently associated with haematological and biochemical abnormalities showing anaemia, leucopenia and thrombocytopenia along with derangement in liver enzymes and decrease in renal function test. Prolonged prothrombin time and abnormal peripheral smear are also seen in these patients. It is associated with increased morbidity and mortality. In our study, haematological parameters (Hb, RBC, PCV MCHC, platelet, PT) all were decreased except MCV and MCH which were increased. However, MCH was statistically not increased. MCV was reduced significantly and biochemical parameters like deranged liver function test were all increased except total protein, albumin and renal function test. S. Urea and Creatinine were reduced. Thus, the complete blood count picture had shown the picture of anaemia, leucopenia and thrombocytopenia. Highly significant p values <0.001 were seen.

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