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Study to evaluate the haematological profile of patients with chronic liver disease

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Abstract

Background: The liver plays an important role in homeostasis. Chronic liver diseases (CLDs), including cirrhosis, hepatic failure, jaundice, and portal hypertension, may affect hemopoiesis. The abnormalities in red blood cells (RBC), white blood cells (WBC), and platelet functions in patients with CLD are well-documented. It is thus important to detect and manage these abnormalities to reduce the overall morbidity and mortality of patients with CLD.
Aims: The study was conducted to assess the hematological abnormalities and hemostatic derangements and the nature of hematological abnormalities to reduce morbidity. Broadly, the hematological abnormalities are viewed under abnormalities in RBCs, WBCs, platelets, and the coagulation profile.

Methods: This was a prospective study conducted for 2 years at the Department of General Medicine, Al Ameen Medical College, Bijapur, Karnataka. A total of 150 patients with CLD were included and analyzed for hematological dysfunction.

Results: Severe anemia (<6g/dL) was noted in 9.33% of the cases; 22% of the cases had 6.1 to 8 g/dL Hb (hemoglobin) levels; 38% cases showed Hb of 8.1 to 10 g/dL; and >10 g/dL HB was noted in 45% cases. The majority showed normocytic normochromic anemia on peripheral smear examination, i.e., 56%. Macrocytic anemia was noted in 25.3% of cases. Microcytic hypochromic anemia was found in 38% of the cases. Only 4.67% showed dimorphic anemia. Besides, 66.6% of cases had a WBC count of 4000-11000/cumm, 26.6% had 2000-4000/cumm, 6.67% had < 2000/cumm, and 59% cases had >1 .0 lakh /cumm. In 66.67% of cases,1 lakh – 50000 (mild thrombocytopenia) was noted in 25.3% of cases. Moreover, 6.6% had moderate thrombocytopenia, and 1.3% < 20000 /cumm (severe thrombocytopenia).

Conclusion: This study demonstrated that all the patients presented with signs of CLD must be thoroughly evaluated for their complete blood profile to detect hematological abnormalities and should be monitored for any complications. Early initiation of treatment can decrease the overall mortality in these patients.

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Highlights

What is current knowledge?

Chronic liver diseases are frequently associated with hematological abnormalities, and the etiology of liver cirrhosis is multifactorial. This study evaluated the hematological profile of patients with chronic liver disease.

What is new here?

Microcytosis occurred in patients with bleeding tendencies, and macrocytosis occurred mostly in alcoholics. Leukopenia was noted in 6.67% of cases who had a WBC count of < 2000/cumm and 1.3% of those with < 20000 /cumm (severe thrombocytopenia).

Introduction

The liver is the largest organ in the body and one of the most complex functioning organs with a wide array of functions. It plays a major role in carbohydrate, protein, and lipid metabolism; inactivation of various toxins; metabolism of drugs and hormones; synthesis of plasma proteins; and maintenance of immunity (Kupffer cells). From being a primary site of hematopoiesis in fetal life to the maintenance of hematological parameters in postnatal life, the liver has an extremely important role in the maintenance of blood homeostasis. It acts as a storage depot for iron, folic acid, and vitamin B12 and secretes clotting factors and inhibitors. Hence, it is not surprising to see a wide range of hematological abnormalities in liver diseases. In chronic liver disease (CLD), the presence of jaundice, liver cell failure, portal hypertension, and hypersplenism, as well as reduced red cell half-life, all influence the peripheral blood picture. Both liver cell failure and cholestasis can derange the coagulation system. Dietary deficiencies, bleeding, alcoholism, and abnormalities in the hepatic synthesis of proteins used for blood formation or coagulation add to the problem of liver disease (1).

Chronic liver diseases are frequently associated with hematological abnormalities. Anemia occurs in about 75% of patients with chronic liver disease (2). The most common type of anemia seen in liver cirrhosis is normocytic normochromic anemia due to the chronic inflammatory state. Blood loss from esophageal and rectal varices, portal hypertensive gastropathy, and antral vascular ectasia can give rise to iron-deficiency anemia (microcytic hypochromic anemia) (3,4). Secondly, the functional and structural defects in the membrane of red blood cells (RBCs) lead to acanthocytes and reduced life span. Another reason for anemia in patients with chronic liver disease is hypersplenism and hepcidin deficiency. A common hematological abnormality seen in chronic liver disease patients is macrocytosis (5). The cause of macrocytosis in liver cirrhosis is multifactorial. This study aimed to assess the hematological profile of patients with chronic liver disease.

Methods

This hospital-based cross-sectional study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all the cases. This study was conducted at the Department of Medicine, Al Ameen Medical College, Bijapur, Karnataka, for 2 years, from August 2020 to July 2021, on 150 patients admitted to the hospital for evaluation of chronic liver disease.

Based on the literature, the prevalence of hematological abnormalities in cases of CLD is approximately 80% (1). Sample size was calculated using the following formula: $n = Z_{\alpha}^2$ (5%) p (1-p) / E^2

n= sample size
Z = level of significance (At 95% confidence level, its value is 1.96.)
P = probability (0.80)
Q = 1-P (1-0.80=0.20)
E= error (10% of prevalence)
$n = (1.96)^2 * (0.80)* (0.20) / (0.08)^2$
n =100 (approx.)

Inclusion Criteria: Age of 18 years to 60 years, both sexes, with signs and symptoms of chronic liver disease persisting for more than 6 months.
Exclusion Criteria: Patients with underlying malignancy or known primary hepatocellular carcinoma, primary coagulation disorder or primary abnormalities of hemostatic function, acute hepatic failure, end-stage medical diseases such as chronic obstructive pulmonary disease (COPD), coronary artery disease, cardiac failure, and chronic kidney disease (CKD), and pregnant women with CLD.

Demographic data included age, sex, occupation, area of residence, and history of present illness (duration of illness, bleeding tendencies, abdominal distension, jaundice, oliguria). History was taken regarding previous treatment of diabetes, hypertension, tuberculosis, coronary heart disease, trauma, blood transfusion, surgery needle pricks, and contact with blood products. Personal

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history regarding alcoholism and smoking and family history of chronic liver diseases, Haypertesion and Diabetes mellitus (DM)were also taken. Three sets of blood samples were taken and sent to the Departments of Pathology (for hematological investigations), Biochemistry (for biochemical investigations) and Microbiology for serological investigations. Patients were evaluated for chronic liver disease to establish the diagnosis of cirrhosis. After establishing the diagnosis, the patients were evaluated for hematological abnormalities.

All the blood samples from the patients were sent to respective departments for related investigations. All the basic biochemical and pathological investigations were performed. If necessary, other investigations, such as abdominal paracentesis**,** liver biopsy, and upper gastrointestinal (GI) endoscopy were performed.

The collected data were coded and entered into a Microsoft Excel for Mac (Version 16.16.27-201012). The data were analyzed in SPSS (Statistical Package for Social Sciences) v. 25.0 software (IBM Corp., Armonk, NY, USA). The results are presented in tabular and graphical formats. For qualitative data, various rates, ratios, and percentages (%) were calculated. For quantitative data, mean/median, standard deviation (SD), etc. were calculated. The chi-square test/Fisher's exact test was used to find the association between 2 or more attributes for qualitative data variables.

Unpaired *t*-test/Mann-Whitney U test was used to compare the 2 independent groups for quantitative variables.

An analysis of variance (ANOVA)/Kruskal-Wallis test was used to compare 3 or more independent groups for quantitative data. P-value < 0.05 was considered significant.

Results

In the present study, the age ranged from 18 years to more than 70 years. The majority belonged to the 31-40 –year age group, constituting 30% (30/100), followed by 51-60 (25%, 25/100). Besides, 22% (22/100) aged 41-50 years and 12% (12/100) aged 18-30 years. Only one case was 75 years old. Males were predominant (80%) compared to females (20%).

The majority of the patients presented with abdominal distension (70.6%), followed by generalized weakness (64%). Fever was noted in 42.6% of cases. Dyspnea was found in 39.3% of cases. Moreover, 61.3% had hematemesis/melaena, and bleeding manifestations were observed in 74.6% of the cases. Abdominal pain was seen in 67.3% of cases. Pallor was found in 40% of cases and icterus in 67.3%. Besides, 60% of cases were alcoholic, and about 40% were nonalcoholic. The most common diagnosis was alcoholic liver disease and decompensated CLD in 32.6% of cases and 11.3% of cases, respectively. Diabetes was noted in 12% of cases, and Hepatitis B Surface Antigen (HbsAg) in 6% of cases.

Severe anemia (<6 g/dL) was noted in 9.33%. Besides, 22% of cases had 6.1 to 8 g/dL Hb levels, 38% of cases showed Hb of 8.1 to 10 g/dL, and >10 g/dL Hb was noted in 45% of cases.

The majority showed a normocytic normochromic anemia picture on peripheral smear examination (56%). Macrocytic anemia was observed in 25.3%. Microcytic hypochromic anemia was seen in 38% of cases, and only 4.67 % of cases showed dimorphic anemia. Moreover, 66.6% cases had WBC count of 4000-11000/cumm, 26.6% had 2000-4000/cumm, 6.67% cases had < 2000/cum, 59% cases had >1 lakh /cumm.

Discussion

In the present study, the age ranged from 18 years to more than 70 years. The majority belonged to 31-40 years, constituting 30% (30/100), followed by 51-60 years. In Selvamani et al.'s (6) study, most of the patients were in the middle age group, and only 6% were younger. In Bibhu Prasad Behera et al.'s (7) study, the average age of the patients was 49.8±13.19 years. In Sudhir Chandra Jha et al.'s (8) study, most of the patients were aged 31-50 years. In Shivam Khare et al.'s (9) study, the mean age of all patients was 47.56±13.77 years. The mean age of males was 48.708±12.36 years, and that of females was 44.607±16.74 years. The mean age of alcoholic and nonalcoholic patients was 47.07±10.92 years and 47.96±15.81 years, respectively. In Jasmine et al.'s (10) study, 78 (86.6%) out of the 90 patients were men and 12 (13.3%) patients were women. The mean age was 52.67 years. Rajkumar et al. (11) reported that the age range was from 24 to 70. The average age of the patients in the study was 48 years, and 70% of the patients were between 40 and 60 years of age.

In the present study, males were predominant (80%) compared to females (20%). In Bibhu Prasad Behera et al.'s (7) study, out of 69 patients, 59 (85.51%) were male, and 10 (14.49%) were female, with a male-to-female ratio of 5.9:1.

In our study, the most common diagnosis was alcoholic liver disease and decompensated CLD in 32.6% and 11.3% of cases, respectively. In Sudhir Chandra Jha et al.'s (8) study, the most common etiology for chronic liver disease was alcohol, followed by chronic hepatitis B. In Selvamani et al.'s (6) study, out of 6 patients, 2 were diagnosed with Wilson's disease, and the others were of unknown etiology. The remaining 94 patients were diagnosed with chronic decompensated liver disease with pathology as cirrhosis and were of variable etiology. According to Jasmine et al. (10), alcohol was the most common etiology of cirrhosis in 52 patients (57.8 %), followed by hepatitis C in 16 patients (17.8%), both alcohol and hepatitis C virus (HCV) in 10 patients (11.1%), hepatitis B in 6 patients (6.6%), and other etiologies in 6 patients (6.6%). The signs and symptoms on presentation were fatigue, abdominal distention, abdominal pain, fever, upper gastrointestinal hemorrhage, pedal edema, jaundice, hepatomegaly, and splenomegaly. Abdominal distention (92.8%) and fatigue (88.8%) were the most common presenting symptoms. According to Raj Kumar et al. (11), the etiology of chronic liver disease could not be determined in 24% of the cases, but all of them had clinical and radiological features of cirrhosis. Six patients had hepatitis B, and 2 had hepatitis C; all these 8 patients had cirrhosis. Autoimmune hepatitis and cirrhosis were present in 2 females.

In the present study, 60% of the cases were alcoholic, and about 40% were nonalcoholic. In Selvamani et al.'s (6) study, among 20 female patients, none gave a history of alcoholism, and among the 80 male patients, 62 patients were found to be alcoholics. In Bibhu Prasad Behera et al.'s (7) study, 92.75% of the patients were alcoholics. Out of 10 females, 9 gave a history of alcoholism, and out of 59 males, 55 were alcoholic.

In our study, 15.3% of the cases had jaundice. In Selvamani et al.'s (6) study, among 100 patients, only 32 patients had a history of jaundice. Later serologic investigations for HBV Ag. anti-HCV antibody showed 12 patients positive for HBS Ag and 2 patients positive for anti-HCV antibody.

In the present study, the majority of the patients presented with abdominal distension (70.6%), followed by generalized weakness (64%), fever (42.6%), and dyspnea (39.3%). Moreover, 61.3% had hematemesis/melaena, and bleeding manifestations were seen in 74.6%. Abdominal pain was found in 67.3% of cases, pallor in 40%, and icterus in 67.3%. In Selvamani et al.'s (6) study, among the 100 patients, 100% had anorexia, weakness, and fatigability. Jaundice was found in 60%. The bleeding tendency was seen in 30%. In Bibhu Prasad Behera et al.'s (7) study, abdominal distension (92.75%) and ascites (84.06%) were the most common presenting complaints. Pallor was present in 42 (60.87%) cases. Splenomegaly was present in 35 (50.72%) patients with liver cirrhosis. Renal dysfunction was present in 23 (33.33%) cases. Four (5.8%) patients presented with hematemesis and/or melena. One (1.45%) presented with hepatic encephalopathy.

In the present study, severe anemia (< 6g/dL) was noted in 9.33% of cases; 22% of cases had 6.1 to 8 g/dL Hb levels; 8% of cases showed Hb of 8.1 to 10 g/dL; and >10 g/dL Hb was noted in 45% cases (Table 1). Sudhir Chandra Jha8 reported that 88% of patients were anemic, out of which 24% of patients were severely anemic. In Selvamani et al.'s study, 88 patients had anemia, and only 12 patients had normal hemoglobin above 12 gm%. About 32 patients had severe anemia (less than 8 gm%). Bibhu Prasad Behera p7) showed the hematological profile of cirrhosis of liver patients with a mean Hb of 7.99±2.18 g/dL, of whom 62 (89.85%) patients had Hb <11 g/dL, among which 37 (53.62%) had Hb ⩽8 g/dL. Bibhu Prasad Behera (7) showed that 66 (95.65%) patients had anemia. Only 03 patients had Hb within the normal range. In Awasthi et al.'s (12) study, the mean hemoglobin, platelet counts, total leukocyte count, and MCV were 10.215 ± 3.339 g/dL, 140627 ± 89899/µL, 10063 ± 5432.7 cumm, and 90.501 ± 11.63 fl, respectively. Anemia (<11 g/dL), raised total leukocyte count (more than 11000 cumm), low platelet count (<150,000/µL), and raised MCV (more than 96 fl) were seen in 75%, 62%, 36%, and 42% of the patients, respectively. In Jasmine et al.'s study10, the mean Hb level was 8.8 g/dL (Table 2)

Table 1. Association of HB with CLD

Hb%	CLD Present	CLD Absent	X^2 VALUE, P-Value
< 6 gm%	9 (50%)	9 (50%)	0.449, 0.9
6-8 gm%	17 (44.7%)	21 (55.3%)	
8.1- 10gm%	23 (44.2%)	29 (55.8%)	
> 10gm%	21 (50%)	21 (50%)	

HB: Hemoglobin; CLD: Chronic liver disease
Hemoglobin count was not significantly associated with chronic liver disease (P=0.9).

Table 2. Correlation of MCV and CLD

MCV	CLD Present	CLD Absent	X2 VALUE, P-value
< 80	27 (58.7%)	19 (41.3%)	4.15, 0.1
80-100	37 (42.5%)	50 (57.5%)	
>100	06 (35.3%)	11 (64.7%)	

MCV: Mean corpuscular volume; CLD: Chronic liver disease
MCV was not significantly associated with chronic liver disease (P=0.1).

In the present study, the majority showed a normocytic normochromic anemia picture on peripheral smear examination (56%). Macrocytic anemia was noted in 25.3% of cases. Microcytic hypochromic anemia was seen in 38% of cases. Only 4.67% of cases showed a dimorphic anemia picture. In Selvamani et al.'s (6) study, among the 100 patients, 52 patients had normochromic and normocytic anemia, 30 patients had microcytic anemia, 16 patients had macrocytosis, and 2 patients had dimorphic anemia. In Shivam Khare et al.'s (9) study, normocytic normochromic anemia was common in both groups, but in alcoholic CLD, MCV was higher than in nonalcoholic CLD. In Bibhu Prasad Behera.'s (7) study, microcytic hypochromic anemia was predominant in cirrhosis patients. Macrocytic anemias were more common in males.

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In the present study, 66.6% of the cases had WBC count of 4000-11000/cumm, 26.6% had 2000- 4000/cumm, and 6.67% had < 2000/cumm (Table 3). In Selvamani et al.'s (6) study, among the 100 patients, leucocytosis was observed in 22 patients. Eosinophilia was found in 2 patients. Leukopenia was present in 6% of the patients.

Table 3. Association of WBC and CLD

WBC Count	CLD Present	CLD Absent	X2 VALUE, P-value
<2000	3(30%)	7 (70%)	6.02, 0.04
2000-4000	25 (62.5%)	15 (37.5%)	
4000-11000	42 (42%)	58 (58%)	

WBC: White blood cells; CLD: Chronic liver disease
The WBC count was significantly associated with chronic liver disease (P=0.04).

In the present study, 59% cases had >1 lakh /cumm in 66.67% of cases; 1 Lakh -50000 (mild thrombocytopenia) was noted in 25.3% of cases; 6.6% had moderate thrombocytopenia; 1.3% < 20000 /cumm (severe thrombocytopenia) (Table 4). In Selvamani et al.'s (6) study, thrombocytopenia was found in 46 patients among 100 cases. Severe thrombocytopenia of <50,000 cell/mm3 was found in patients with large spleen >8 cms who had a history of massive hematemesis. Bibhu Prasad Behera et al.'s (7) study showed that 47 (68.12%) of the patients had decreased platelet count, out of whom 23 (33.33%) patients had <1.0 lakh/mL platelet count. In Rajkumari et al.'s (11) study, 50% of the patients had thrombocytopenia (<1 lakh /cumm); of the 13 patients who had upper GI bleeding, 3 patients had normal platelet counts, and the rest had counts below 1 lakh. The average platelet count of the patients who experienced an upper GI bleed was 92000 vs. 1.2 lakh in patients without GI bleeding.

Table 4. Correlation of Platelets and CLD

Platelet Count	CLD Present	CLD Absent	X2 Value, P-value
< 20,000	4 (100%)	0	8.85, 0.03
20,000 - 50,000	2 (20%)	8 (80%)	
50,001-1,00,000	18 (56.2%)	14 (43.8%)	
> 1,00,000	46 (44.2%)	58 (55.8%)	

CLD: Chronic liver disease
Platelet count was significantly associated with chronic liver disease (P=0.03).

Conclusion

The most common anemia was normochromic normocytic anemia. Microcytosis occurred in patients with bleeding tendencies, and macrocytosis occurred mostly in alcoholics. Leukopenia was noted in 6.67% of the cases who had a WBC count of < 2000/cumm and in 1.3% with < 20000 /cumm (severe thrombocytopenia).

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Ethical statement

The study protocol was approved by the Ethical Committee of the institute.

Conflicts of interest

There are no conflicts of interest.

Author contributions

All the authors had the same contribution.

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