J MEDICINE 2024; 25: 41-45

Original Article

Red Cell Indices in Chronic Liver Disease

Rafiya Afroz[1], Sudip Ranjan Deb[2], Ahmedul Kabir[3]

Abstract:

Background: *Chronic liver disease (CLD) in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis. Liver diseases are frequently associated with hematological abnormalities. Bleeding and defective blood coagulation contributes to the anemia in CLD patients. Other mechanisms of anemia include aplastic anemia secondary to previous hepatitis, or side effects of treatment of hepatitis with chemotherapeutic agent. Other different factors, such as malabsorption, malnutrition or direct toxic effect also contribute to hematological abnormalities. The examination of complete blood count is common, economically cheap and readily available laboratory procedure. Red cell indices are valuable in the evaluation of morphologic characteristic of anaemias or hematological abnormalities in CLD patients.*

Objectives*: To assess the red cell indices in chronic liver disease patients.*

Materials & method: *This descriptive type of cross-sectional study was conducted in Department of Medicine, Dhaka Medical College Hospital, Dhaka, among 75 cases of Chronic liver disease patients. Samples were selected by purposive sampling technique. Detail demographic data were collected from the patients and recorded in structured case report form. Clinical examination and relevant investigation were done meticulously. Data was processed and analysed with the help of computer program SPSS and Microsoft excel. Quantitative data expressed as mean and standard deviation and qualitative data as frequency and percentage. Results was presented by tabulation and graphical presentation in the form of tables, pie chart, graphs, bar diagrams, histogram & charts etc.*

Result*: Maximum number of patients, 37(49.3%) were between 31-40 years of age with mean age of the patient was 37.58 ± 8.23 years. Out of 75 cases 58(77.0%) patients were male and 17(23.0%) were female. Male-female ratio was 3.34:1. Majority of patients belonged to Child Pugh score B. Prevalence of anaemia was 54(72%) in CLD patients. Microcytic anaemia was predominant and Normocytic anaemia was second most common. Hb concentration & MCV decreases with the severity of Child Pugh score. Abnormalities of red cell indices were positively associated with severity of CLD.*

Conclusion*: Present study concluded that chronic liver diseases are associated with hematological abnormalities. Patients with severe hepatocellular disease develop defects of blood coagulation as a consequence of endothelial dysfunction, thrombocytopenia, deficiencies of coagulation factors and various associated disorders. In overall patients, Child Pugh class C cases had significant low hemoglobin in comparison to rest of group. Assessing the severity and type of anaemia by red cell indices is a useful tool for proper treatment, prognosis in patients of CLD for reducing the mortality and morbidity.*

Key words: *Red Cell Indices, Chronic Liver Disease*

DOI: *https://doi.org/10.3329/jom.v25i1.70525*

Received: *4.11.2023;* ***Accepted:*** *18.12.2023*

1. Indoor Medical Officer, Department of Medicine, Shaheed Suhrawardy Medical College Hospital, Dhaka
2. Associate Professor, Dept. of Medicine, Dhaka Medical College Hospital
3. Additional Directorate General, Planninng, DGHS

Corresponding author: Dr. Rafiya Afroz, email: ripak65@gmail.com, Phone: 01729564645

Introduction:

Chronic liver diseases (CLD) are leading causes of morbidity and mortality in developed and developing country. Chronic liver diseases (CLD) are defined by the following triad: 1) prolonged course of a hepatic disease >6 months; 2) inflammatory and/ or degenerative morphological findings;

and 3) uncertain prognosis[1]. Cirrhosis results from end stage chronic liver disease, and is characterized by advanced fibrosis, scarring, and formation of regenerative nodules leading to architectural distortion. It is a leading cause of morbidity and mortality around the world[2]. Regardless of the etiology of cirrhosis, the development of portal hypertension is nearly universal and results from an increased resistance to portal flow secondary to scarring, narrowing, and compression of the hepatic sinusoids. When the portal pressure exceeds a certain threshold, it results in the development of varices[3] and other complications, like hematological abnormalities, anaemia.

The natural history of chronic liver disease in a subset of patients is progression to cirrhosis. Cirrhosis has two broad stages. The onset of jaundice, ascites, variceal bleeding, or hepatic encephalopathy heralds the onset of decompensated cirrhosis; the stage where there is absence of any of these complications is compensated cirrhosis[4]. The liver is involved in or is responsible for various nutritional, hematological and ionic abnormalities due to its unique portal circulation and its synthetic, excreatory and hemostatic functions.

Primary liver problems like cirrhosis can lead to hematological abnormalities and primary hematological diseases can in turn affect the liver and its functioning. Anaemia in liver disease may be secondary to a variety of factors including nutritional deficiency of iron, folate, Vitamin B_{12} and B_6. Blood loss secondary to variceal bleeding (always overt bleeding), portal hypertensive vasculopathy (may be overt or occult bleeding) and duodenal ulcer (more common in patients with cirrhosis) is also common factors. Other causes of anaemia are anaemia of chronic disease and hemolysis[5].

In severe hepatocellular disease, decreased synthesis of liver-produced plasma proteins leads to reduced serum levels of several blood clotting factors. Hemorrhage may occur as a complication of chronic liver disease because of a lack of one or more liver-produced blood clotting factors, thrombocytopenia and/or defective platelet function. Hemorrhage in such patients may also occur from esophageal or gastric varices secondary to portal hypertension. The biosynthetic pathways of blood coagulation factors II, VII, IX and X are within the hepatocyte and are dependent on vitamin K[6, 7]. Low serum levels of these factors are associated with prolongation of the prothrombin time (PT).

Another factor splenomegaly, which is usually caused by portal hypertension in patients with chronic liver disease, may lead to secondary hemolysis, an increase in plasma volume, macrocytosis and megaloblastic anemia. Anemia is alao recognized complication of treatment of chronic hepatitis with a combination of interferon and ribavirin or other chemotherapeutic agent[8]. Therefore evaluations of complete blood count and red cell indices are important part of assessment of hematological abnormalities in CLD.

In clinical practice, liver disease and its severity is commonly assessed by several tests like biochemical tests of LFT, USG, endoscopy of GIT, colonoscopy, etc. Theses test are invasive, costly, time consuming & technical orientated and all tests are not available in primary or secondary health care centre. But CBC or red c3ell indices are common hematological tests, available in all level of heath care centre. Red blood cell (RBC) indices are part of the complete blood count (CBC) test. The indices include: average red blood cell size (MCV), hemoglobin amount per red blood cell (MCH), amount of hemoglobin relative to the size of the cell (hemoglobin concentration) per red blood cell (MCHC). These parameters alter in progression of disease. Early detection and treatment of haematological changes can prevent complications and reduce the mortality in CLD patients[9].

Materials & Methods:

This descriptive type of cross-sectional study was conducted in Department of Medicine, Dhaka Medical College Hospital, Dhaka. Patients of chronic liver disease were enrolled according to selection criteria. Sample was selected by purposive sampling technique. The case of clinical cirrhosis was defined as a patient having clinical feature of haematemesis and/ or melaena, ascities with or without splenomegaly, testicular atrophy (in case of male) along with ultrasound (USG) findings suggestive of cirrhosis of liver. Patients on drugs which influence RBC indices such as glucocorticoid, synthetic estrogen, aspirin, tamoxifen, methotrexate, OCP etc and patients of CLD with hepatocellular carcinoma, seriously, terminally ill patients, or preexisting haematological and coagulation disorder were excluded from study. After fulfilling the inclusion and exclusion criteria, patient were enrolled with unique ID. Patient demographic data and clinical presentation etc were noted. As a routine, a sample of blood (10 ml) was collected & sent to the clinical pathology, biochemistry laboratory for haematological and for other test. Hematological value and Red blood cell indices were measured according to reference value. Patients were monitored & follow-up after treatment and outcome was measured accordingly. All the information

recorded in data collection sheet. Data was processed and analysed with the help of computer program SPSS and Microsoft excel. Quantitative data expressed as mean and standard deviation and qualitative data as frequency and percentage. Result was presented by tabulation and graphical presentation in the form of tables, pie chart, graphs, bar diagrams, histogram & charts etc.

Result:

Table 1. *Demographic characteristics of the patients (n=75)*

Variables	Frequency	Percentage
Age (years)		
21-30	16	21.3%
31-40	37	49.3%
41-50	20	26.6%
>50	2	2.6%
Mean ± SD	37.58 ± 8.23	
Gender		
Male	58	77.0%
Female	17	23.0%
Residence		
Rural	32	42.6%
Urban	43	57.4%

Maximum number of patients, 37(49.3%) were between 31-40 years of age. Mean age of the patient was 37.58 ± 8.23 years. Out of 75 cases 58(77.0%) patients were male and 17(23.0%) were female. Male – female ratio was 3.34:1. Large numbers of respondents came from urban area (e.g., 57.4%) Table 1.

Table 2. *Evaluation of severity of CLD by Child-Pugh score (CPS) classification (n=75)*

CPS Class	Frequency	Percentage (%)
A	17	22.6%
B	35	46.6%
C	23	30.6%

The severity of CLD was calculated by Child-Pugh score (CPS) classification. Majority of patients (46.6%) belonged to Child Pugh score B. Child pugh score C were 23(30.6%) patients Table 2.

Table 3. *Hemoglobin level of study subject and its association with CLD severity (n=75)*

Hb level	CPS A	CPS B	CPS C
≤8 mg/dl	2(11.76%)	4(11.42%)	9(39.13%)
8.1-11.4 mg/dl	6(35.29%)	23(65.71%)	10(43.47%)
>11.5 mg/dl	9(52.94%)	8(22.85%)	4(17.39%)
Mean ± SD	9.26 ± 1.3		

In maximum patients (e.g., 52%) haemoglobin concentrations was 8.1-11.4 mg/dl. Study demonstrated that hemoglobin concentration was proportionately reduced with progression of CPS class. In child Pugh class C, 10(43.47%) patients had hemoglobin 8.1-11.4 and 10(43.47%) patients had hemoglobin less than 8. In contrary, majority patients 9(52.94%) of CPS A had haemoglobin more than 11.5 mg/dl Table 3.

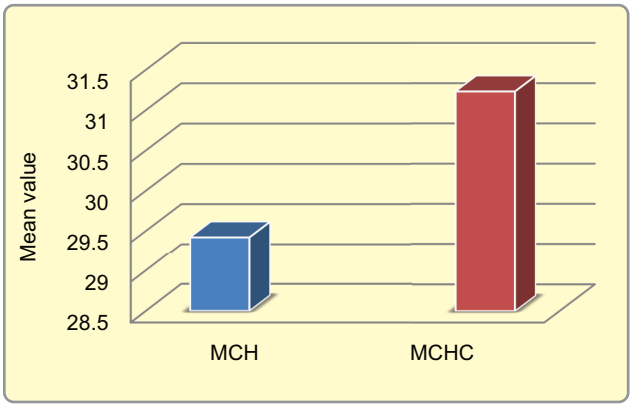

Figure- 1: *Mean value of MCH and MCHC (n=18)*

Mean value of MCH (mean corpuscular haemoglobin) was 29.42 pg. Mean value of MCHC (mean corpuscular haemoglobib concentration) was 31.23 g/dl Figure 1.

Table 4. *Evaluation of the MCV and its association with CLD severity (n=75)*

MCV (fl)	CPS A	CPS B	CPS C
<78 fl	2(11.76%)	16(45.71%)	14(60.86%)
78-98 fl	13(76.47%)	19(54.28%)	6(26.08%)
>98 fl	2(11.76%)	0	3(13.04%)

Normal mean cell volume (MCV) is 78-98 fl. Present study shows that 26(34.66%) of CLD patients detected reduced MCV (MCV is less than 78 fl), few number of patients 4(5.33%) shows elevated MCV (MCV more than 98 fl), remaining 45 cases were within normal limit. Child Pugh class C patients were comparatively more in number 10(43.47%) with reduced MCV Table 4.

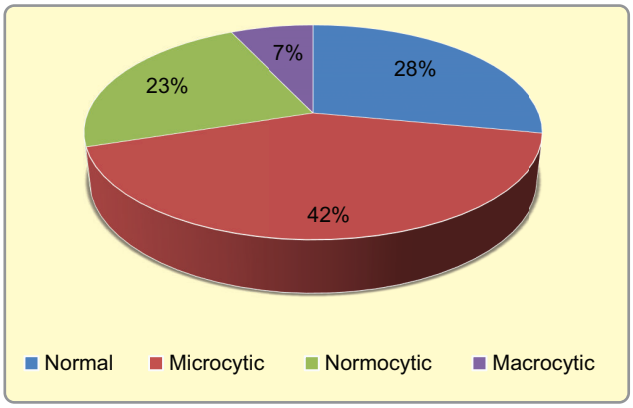

Figure- 2: *Prevalence and pattern of anaemia according to RBC indices in CLD patient (n=75)*

Present study demonstrated that prevalence of anemia is 72% in chronic liver disease patients. Red blood cell absolute value was evaluated meticulously in every patient. Among the pattern of anemia microcytic was more common 32(42%) Figure 2.

Discussion:

In this study maximum number of patients, 37(49.3%) were between 31-40 years of age. Mean age of the patient was 37.58 ± 8.23 years. Findings are consistent with result of other study. Study in a tertiary care hospital, Dharan, Nepal reported that the mean age of the patients was 49.06 ±11.27 years (range 23-73 years). Ninety patients were adult cirrhotics (age ≥35 yrs) and the remaining 15 patients were young (age ≤35 yrs)[10]. It is generally believed that cirrhosis occur much less frequently in young adults than in older patients. A number of reports from the West and Japan, it was found that less than 5% of cirrhosis was under 30-35 years of age[11]. In India, however 37% were patients of ≤35years[32].

In this study out of 75 cases 58(77.0%) patients were male and 17(23.0%) were female. Male-female ratio was 3.34:1. Another study reported that, in overall CLD cases, Males are predominant with 72%, mean age of all patients was 47.56±13.77 years[9]. In a study done in Nepal done by Om K Pathak et al (2009)[13] 181 patients were analyzed out of which 146 males and 35 are female. Mean age was 52.08 ± 13.11 years. So all report are similar with this study.

In this study majority of patients 39(52%) had haemoglobin concentration 8.1-11.4 mg/dl, followed by 21(28%) of patients were more than 11.5 mg/dl. Study demonstrated that hemoglobin concentration was proportionately reduced with progression of CPS class. In child Pugh class C, 10(43.47%) patients had hemoglobin 8.1-11.4 and 10(43.47%) patients had hemoglobin less than 8. In contrary, majority patients 9(52.94%) of CPS A had haemoglobin more than 11.5 mg/dl. In overall, Child Pugh class C cases had significant low hemoglobin in comparison to rest of group ($p = 0.006$). While in study by E Halleys kumar and colleage (2014)[14], 58% of cases were having Hb < 9.0gm/dl, another study by Khare S et al[9] conform that 49 % were having Hb < 8.0gm/dl in their study.

Several study reported that chronic liver diseases frequently are associated with hematological abnormalities. Anemia of diverse etiology occurs in about 75% of patients with chronic liver disease[15]. A major cause of anemia associated with chronic liver disease is hemorrhage, especially into the gastrointestinal tract. Patients with severe hepatocellular disease develop defects of blood coagulation as a consequence of endothelial dysfunction, thrombocytopenia, deficiencies of coagulation factors and various associated disorders[16].

Present study revealed that Mean value of MCH (mean corpuscular haemoglobin) was 29.42 pg. Mean value of MCHC (mean corpuscular haemoglobib concentration) was 31.23 g/dl. Regarding operational definition normal mean cell volume (MCV) is 78-98 fl. Present study shows that 26(34.66%) of CLD patients detected reduced MCV (MCV is less than 78 fl), few number of patients 4(5.33%) shows elevated MCV (MCV more than 98 fl), remaining 45 cases were within normal limit. Child Pugh class C patients were comparatively more in number 10(43.47%) with reduced MCV. Present study demonstrated that microcytic anaemia detected predominantly. Previous study by E Halleys kumar and colleage (2014)[14], reported that normocytic Normochromic anaemia was predominant, second predominant type in patients of CLD was microcytic hypochromic in their study. It may due to presentation and clinical situation of CLD patients varies. In tertiary centre of Bangladesh maximum cases admitted for treatment of CLD related complication like ascites, hepatic encephalopathy, variceal bleeding etc.

According to Sheila sherlock[17] and Oxford text book of hepatology, most common anaemia in seen in cirrhotic patients was normocytic and normochromic anaemia. In

Shigeo Maruyama (2001)[18] study, macrocytosis was mainly found in cirrhotics due to alcoholism. In study by Dr Bijoy kumar Barik (2010)[19]; macrocytosis was present in chronic alcoholism. Present study demonstrated that prevalence of anemia is 72% among chronic liver disease patients. Hence, proper evaluation of RBC indices can helps to accurate monitoring, management, prognosis of chronic liver disease.

Conclusions:

It has been well established that many haematological and biochemical abnormalities occur in chronic liver diseases. Hb concentration & MCV decreases with the severity of Child Pugh score so we can say that as severity of CLD increases it directly aggravates anaemia. Observations showed that most of the patients of Child pugh score C had severe anemia. It signifies the fact that anemia can be bad prognostic factor in CLD patients. Assessing the severity and type of anaemia by RBC indices is a useful tool for early initiation of the treatment in patients of CLD for reducing the mortality and morbidity.

References:

1. Kuntz E and Hans-Dieter K. Hepatology, Principles and Practice: History, Morphology, Biochemistry, Diagnostics, Clinic, Therapy. Springer Medizin Verlag 2006 (2nd edition): 691-739.
2. Nusrat S, Khan MS, Fazili J, Madhoun MF. Cirrhosis and its complications: Evidence based treatment. World J Gastroenterol 2014; 20(18): 5442-5460
3. Heidelbaugh J and Sherbondy M. Cirrhosis and Chronic Liver Failure: Part II. Complications and Treatment. Am Fam Physician 2006;74:767-76.
4. Kamath P. Acute on Chronic Liver Failure. Clinical Liver Disease, 2017; 9(4): 86-88.
5. Gupte P and Nagral A. Hematological problems and liver disease. Tropical Gastroenterology 2009;30(2): P 65–70
6. Gisbert JP. Spectrum of anemia associated with chronic liver disease. World J Gastroenterol, 2009 October 7; 15(37): 4653-4658
7. Pereira SP, Langley PG, Williams R. The management of abnormalities of hemostasis in acute liver failure. Semin Liver Dis1996; 16: 403-414
8. Van Vlierbergh H, Delanghe JR, De Vos M, Leroux-Roel G. Factors influencing ribavirin-induced hemolysis. J Hepatol, 2001; 34: 911-916
9. Khare S, Garg V, Jain H and Jatav O. To study haematological profile in patients of chronic liver disease. International Journal of Multidisciplinary Research and Development. Aug 2015, Volume: 2, Issue: 8, P 378-381.
10. Maskey R, Karki P, Ahmed SV, Manandhar DN. Clinical profile of patients with cirrhosis of liver in a tertiary care hospital, Dharan, Nepal. Nepal Med Coll J 2011; 13(2): 115-118.
11. Yoshida T, Kawata H, Fukui O, Koizumi T, Asada M, Wada M. Cirrhosis of liver in Japan. Acta Hepatolosplenol1965;12: 268-78.
12. Sarin SK, Chari S, Sundaram KR, Ahuja RK, Anand BS, Broor SL. Young versus adult cirrhosis: a prospective comparative analysis of the clinical profile, natural course and survival. Gut1988; 29: 101-7.
13. Om K. Pathak, Raju Paudel, Baikuntha Adhikari. Retrospective Study of the Clinical Profile and Prognostic Indicators in Patients of Alcoholic Liver Disease Admitted to a Tertiary Care Teaching Hospital in Western Nepal Saudi Journal of Gastroenterology: Official Journal of the Saudi Gastroenterology Association.
14. Halleys Kumar E, Radhakrishnan A. Prevalence of Anaemia in Decompensated Chronic Liver Disease World Journal of Medical Sciences. 2014; 10(1):56-60.
15. McHutchison JG, Manns MP, Longo DL. Definition and management of anemia in patients infected with hepatitis C virus. Liver Int2006; 26: 389-398
16. Caldwell SH, Hoffman M, Lisman T, Macik BG, Northup PG, Reddy KR, Tripodi A, Sanyal AJ. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. Hepatology 2006; 44: 1039-1046
17. Sheila Sherlock. Diseases of the Liver and Biliary System Eleventh Edition.
18. Shigeo Maruyama, Chisato Hirayama, Satoru Yamamoto, Masahiro Koda, Akihiro Udagawa, Yoshiro Kadowaki. Red blood cell status in alcoholic and non-alcoholic liver disease Department of Internal Medicine, Saiseikai Gotsu General Hospital. Shimane, Japan Received 22 March 2001; received in revised form 29 May 2001; accepted 1 August 2002.
19. Dr. Bijoykumar Barik. Haematological changes in chronic alcoholic liver disease. 21st July 2010.