PREVALENCE AND PATTERN OF ANEMIA AMONG THE HOSPITALIZED PATIENTS OF CHRONIC LIVER DISEASE IN A TERTIARY CARE HOSPITAL

Abul Faisal Md Nuruddin^{1*} Afreen Sultana² Farhana Akter³ Ershad Uddin Ahmed⁴ Biswajit Dutta⁵

Background : Among the different complications of chronic liver diseases, anemia is not uncommon. This study is done to evaluate the frequency and pattern of anemia among the patients with Chronic Liver Disease (CLD) admitted in a tertiary care hospital of Bangladesh.100 admitted patients of CLD was evaluated for prevalence and pattern of anemia. Materials and methods : Sampling was purposive non random according to inclusion criteria. After clinical evaluation 5 cc venous blood was collected and sent to the Department of Haematology for haematological profile analysis. Male to female ratio was found 3.1:1. From the age distribution of the patients, highest number (45%) was found in the age group of 30-49 years. Results : Hematological abnormality were detected in 85 (85%) of patients. The various abnormality included anaemia (76%) neutropenia (5%) lymphopenia (6%) thrombocytopenia (47%) pancytopenia(5%). Patients had anemia due to various causes including iron deficiency anemia (85.5%) and Anemia of Chronic Diseases (ACD) 11.8%. Fifty percent (50%) patients had severe anemia where Hb was 6.46± 0.9 gm%.

	-	Email: afmchy07@yahoo.com Cell: 01711072347	
*Correspondence:		Dr. Abul Faisal Md Nuruddin	
5.	Associate Professor of Gastroenterology OSD, DGHS, Dhaka.		
4.	Associate Professor of Gastroenterology Chittagong Medical College, Chittagong.		
3.	Assistant Professor of Endocrinology Chittagong Medical College, Chittagong.		
2.	Lecturer of Virology Chittagong Medical College, Chittagong.		
1.	OSD, DGHS, Dhaka.		

Accepted on : 20.12.2017 Accepted on : 24.12.2017 Normocytic normochromic anemia (NNA) was found 30.26%, normocytic hypochromic anemia was found 31.57% and microcytic hypochromic anemia was found 38.15%. **Conclusion :** Liver diseases are frequently associated with hematological abnormalities. Anemia of diverse etiology occurs in many of these patients.

Key words

Chronic liver disease; Anemia; Hematological abnormality.

Introduction

Chronic liver diseases are frequently are associated with hematological abnormalities. Anemia of diverse etiology occurs in about 75% of patients with chronic liver disease¹.

Cirrhosis is usually a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal macro/micronodules. Cirrhosis represents the final histological pathway for a wide variety of liver disease². The progression to cirrhosis is very variable and may occur over several months or many years. Around 80-90% of the liver parenchyma needs to be destroyed before there are clinical signs of liver failure².

A major cause of anemia associated with chronic liver disease and cirrhosis is hemorrhage, especially into the gastrointestinal tract. Patients with severe hepatocellular disease develop defects of blood coagulation as a consequence of endo-thelial dysfunction, thrombocytopenia, deficiencies of coagulation factors and various associated disorders^{2,3}.

In severe chronic liver disease, decreased synthesis of liver-produced plasma proteins leads to reduced serum levels of several blood clotting factors⁴. Anemia due to 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^{5,6}. The biosynthetic pathways of blood coagulation factors II, VII, IX and X are within the hepatocyte and are dependent on vitamin K³. Low serum levels of these factors are associated with prolongation of the Prothrombin Time (PT). When attributable to hepatocellular disease, they are not improved by administration of vitamin K; correction of the associated impaired blood coagulation necessitates infusion of preparations of the deficient factors^{7,8}.

Enlarged spleen usually caused by portal hypertension in patients with chronic liver disease, may lead to secondary hemolysis, an increase in plasma volume, macrocytosis and megaloblastic anemia⁹. Alcohol, a common etiologic factor of chronic liver disease, though uncommon in our country is toxic to the bone marrow. Alcoholics often develop secondary malnutrition, a manifestation of which may be anemia caused by folic acid deficiency¹⁰. In some patients, bone marrow failure and aplastic anemia develop after an episode of hepatitis. Finally, anemia is a recognized complication of treatment of chronic hepatitis C with a combination of interferon and ribavirin: anemia in this context is predominantly caused by ribavirin-induced hemolysis though now a days combination of oral drug are used^{$4, \overline{6}, 7$}.

Association of anemia with chronic liver disease and/or hepatocellular failure provides a rationale for examining the role of the liver in the formation and destruction of erythrocytes^{8,9}. Indeed, the liver itself may be implicated in a variety of different mechanisms that contribute to the development of anemia in patients with chronic liver disease¹¹⁻¹⁴. This study would try to provide an overview of anemia that may complicate chronic liver diseases and the mechanisms responsible So this present study is aimed to evaluate the prevalence and pattern of anemia in our context.

Materials and methods

This is a cross sectional observational study done in Department of Medicine and Gastroenterology, Chittagong Medical College Hospital (CMCH)

from 1st January 2014 to 31st December 2014. One hundred patients admitted in the Department of Medicine and Gastroenterology, CMCH with the diagnosis of CLD as evidenced by clinical, biochemical and serological criteria included in the study. Patient unwilling to give informed consent took blood transfusion within one month of the hospital admission, concomitant other systemic disease was excluded. After written consent, patient was counseled about the objective of the study. All patients were provided with the results of their biochemical, haematological and serological tests and any further information they wished to have. A structured questionnaire was record sociodemographic used to and occupational details, prior symptomatic hepatitis, vaccination status and symptoms related to anemia. Using an aseptic technique, about 5 ml of venous blood was drawn from each participant and immediately put in a vacutainer containing a clot activator. The vacutainers were labeled indicating the serial number and date of sample collection. Blood samples were then taken to the laboratory in the haematology department of CMCH. Peripheral blood film examination and other haematological parameters was analyzed by a single expert haematologist of at least an Assistant Professor level. Statistical analysis were performed with the SPSS software package Statistical Package for Social Sciences (SPSS) for Windows).

Results

Among 100 patients included in the study, 76 (76%) were male and 24(24%) were female. Male to female ratio was found 3.1. From the age distribution of the patients, it was found that highest number of patient i.e. 45 (45%) patients was in the age group of 30-39 years.

Table I : Age group

Age group	Frequency (Percentage)
20-29 years	20 (20%)
30-39 years	45 (45%)
40-49 years	30 (30%)
>50 years	5 (5%)
Total	100



Fig 1 : Clinical features of the patients



Fig 2 : Hematological abnormality

Table II :	Pattern	of Anemia	(n=76)
------------	---------	-----------	--------

Types of anemia	Frequency (Percentages)
IDA	65 (85.5%)
ACD	9 (11.9%)
AIHA	1 (1.3%)
Others	1 (1.3%)
Total	76 (100%)

Among the 100 patients most of the patient 51(51%) had the history of illness for 6-12 years. The most common presenting complaints were jaundice(100%) and weakness and fatigue followed by nausea, vomiting and leg swelling.

Among 100 patients 2 patients were hypertensive at presentation, where as 4 patients had diabetes and 1 had thyroid problem.Hematological abnormality were detected in 85(85%) of patients. The various abnormality included anaemia (76%) neutropenia (5%) lymphopenia (6%) thrombocytopenia (47%) pancytopenia (5%).

Iron deficiency anemia (85.5%) was the most frequent type followed by Anemia of Chronic Diseases (ACD). Fifty percent (50%) patients had severe anaemia where Hb were 6.46 ± 0.9 gm%.

Peripheral blood film examination findings was Normocytic Normochromic Anemia (NNA) in 30.26%, normocytic hypochromic anemia in 31.57% and microcytic hypochromic anemia in 38.15%.

Discussion

This was a cross sectional observational study to see pattern of anemia in 100 patients with Chronic Liver Disease (CLD) done in the Department of Gastroenterology and Medicine at CMCH. There were 100 patients included in the study with 76 (76%) female and 24(24%) males. Male to female ratio was found 3.1: 1. Male are more privileged person in our society and they admit in hospital more commonly then female. So this male predominant distribution is as expected.

It was found that 20 (20%) patient was within 20-29 years of age, 5(5%) within the age group of >50 years. 45 (45%) in the age group of 30-49 years. From the age distribution of the patients, it was found that highest number of patient ie. 45 (45%) patients was in the age group of 30-49 years. As CLD is a chronic disease and it takes more time to make patients to be admitted so in the study most patients are middle aged. Abraldes et al had similar age group of CLD in their study⁶. The most common presenting complaints were jaundice (100%) and weakness and fatigue followed by nausea, vomiting and leg swelling. Among all, 2 patients were hypertensive at presentation where as 4 patients had diabetes and 1 had thyroid problem. Co morbidity is not uncommon in patients with CLD. Similar comorbidity was found in a study done by Albillos¹⁰.

Hematological abnormality were detected in 85(85%) of patients. The various abnormality included anaemia (76%) neutropenia (5%) lymphopenia (6%) thrombocytopenia (47%) pancytopenia (5%). Patients had anemia due to various causes including iron deficiency anemia (85.5%) and Anemia of Chronic Diseases (ACD) 11.8%. Fifty percent (50%) patients had severe anaemia where Hb were 6.46 ± 0.9 gm%.

Normocytic Normochromic Anemia (NNA) was found 30.26%, normocytic hypochromic anemia was found 31.57% and microcytic hypochromic anemia was found 38.15%. These findings are consistent with the earlier study done by Albillos¹⁰.

Anemia of diverse etiology is a common complication of chronic liver diseases. The causes of anemia include acute or chronic gastrointestinal hemorrhage, and hypersplenism secondary to portal hypertension. Severe hepatocellular disease predisposes to hemorrhage because of impaired blood coagulation caused by deficiency of blood coagulation factors synthesized by hepatocytes, and/or thrombocytopenia¹⁵.

Hematological complications of combination therapy for chronic viral hepatitis C include clinically significant anemia, secondary to treatment with ribavirin and/or interferon. Ribavirin-induced hemolysis can be reversed by reducing the dose of the drug or discontinuing it altogether^{16,17}. Interferons may contribute to anemia by inducing bone marrow suppression. But present study did not evaluated the treatment induced anemia as no patient was getting interferon and rivavirin which is one of its potential limitation¹⁵.

Alcohol ingestion is implicated in the pathogenesis of chronic liver disease and may contribute to associated anemia. In patients with chronic liver disease, anemia may be exacerbated by deficiency of folic acid and/or vitamin B_{12} that can occur secondary to inadequate dietary intake or malabsorption. But further evaluation is needed to find out the different contribution factors of anemia in liver diseases.

Limitations

Single center study, small sample size, absence of long term follow up, other causes of blood loss from GIT not excluded and bone marrow study was not done in cytopenic cases.

Conclusion

Anemia in chronic liver disease is a common finding. Among different morphological types, microcytic hypochromic anemia is the commonest.

Disclosure

All the authors declared no competing interest.

References

1. Mc Hutchison JG, Manns MP, Longo DL. Definition and management of anemia in patients infected with hepatitis C virus. Liver Int. 2006; 26: 389–398.

2. Caldwell SH, Hoffman M, Lisman T, Macik BG, Northup PG, Reddy KR et al. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. Hepatology. 2006;44: 1039–1046.

3. Bellentani S, Pozzato G, Saccoccio G. Clinical course and risk factors of hepatitis C virus related liver disease in the general population: report from the Dionysos study. Gut. 1999 ; 44(6):874-880.

4. Van Vlierbergh H, Delanghe JR, De Vos M, Leroux-Roel G. Factors influencing ribavirininduced hemolysis. J Hepatol. 2001;34: 911–916.

5. Farrell GC, Larter CZ, Nonalcoholic fatty liver disease: from steatosis to cirrhosis. Hepatology. 2006; 43(2):S99-S112.

6. Abraldes JG, Bosch J. The treatment of acute variceal bleeding. J Clin Gastroenterol. 2007;41: S312–S317.

7. Kravetz D. Prevention of recurrent esophageal variceal hemorrhage: Review and current recommendations. J Clin Gastroenterol. 2007;41: S318–S322.

8. Jones DE, James OF, Bassendine MF, Primary biliary cirrhosis: clinical and associated autoimmune features and natural history. Clin Liver Dis. 1998; 2(2):265-282.

9. Heidelbaugh JJ, Sherbondy M. Cirrhosis and chronic liver failure: Part II. Complications and treatment. Am Fam Physician. 2006; 74(5):767-776.

10. Albillos A. Preventing first variceal hemorrhage in cirrhosis. J Clin Gastroenterol. 2007; 41 Suppl 3:S305–S311.

11. Laffi G, Marra F, Tarquini R, Abbate R. Coagulation defects in cirrhosis old dogmas not yet ready for burial. J Thromb Haemost. 2006;4: 2068–2069.

12. Lee CM, Leung TK, Wang HJ, Lee WH, Shen LK, Liu JD et al. Evaluation of the effect of partial splenic embolization on platelet values for liver cirrhosis patients with thrombocytopenia. World J Gastroenterol. 2007;13: 619–622.

13. Reverter JC. Abnormal hemostasis tests and bleeding in chronic liver disease: Are they related? Yes. J Thromb Haemost. 2006; 4:717–720.

14. Levy JH, Fingerhut A, Brott T, Langbakke IH, Erhardtsen E, Porte RJ. Recombinant factor VIIa in patients with coagulopathy secondary to anticoagulant therapy, cirrhosis, or severe traumatic injury: review of safety profile. Transfusion. 2006;46:919–933.

Original Article

15. Rosario GC, Jones AE, and Moreno-Otero R. Spectrum of anemia associated with chronic liver disease. World J Gastroenterol. 2009; 15(37): 4653–4658.

16. Ong JP, Younossi ZM. Managing the hematologic side effects of antiviral therapy for chronic hepatitis C: Anemia, neutropenia, and thrombocytopenia. Cleve Clin J Med. 2004;71 Suppl 3:S17–S21.

17. Reau N, Hadziyannis SJ, Messinger D, Fried MW, Jensen DM. Early predictors of anemia in patients with hepatitis C genotype 1 treated with peginterferon alfa-2a (40KD) plus ribavirin. Am J Gastroenterol. 2008;103:1981–1988.