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General

A Study of Spectrum and Prevalence of Anaemia in Patients of Decompensated Chronic Liver Disease in a Rural Tertiary Care Centre in North India

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Abstract: Anaemia is a frequently observed manifestation during clinical course of chronic liver disease. This study was planned to assess the prevalence and spectrum of anaemia in decompensated chronic liver disease patients in a rural tertiary health care centre in north India. One hundred patients were selected in random for this study, from patients coming to department of general medicine OPD and ward patients. Patients of liver disease whose symptoms and signs persisted for more than six months and having signs of decompensated liver disease like ascitis, Variceal bleeding and hepatic encephalopathy were included in the study. Alcoholic, post infective, metabolic causes of liver diseases were taken into consideration. The patients underwent relevant investigations to find the severity and typing of anemia. The mean age of the patients was 44±14 years. The male/female ratio was 4.9/1.The mean Hb value was 9.5±1.92g/dl. The mean MCV was 89.2±11.02fl. 87% patients of decompensated chronic liver disease in our study were anaemic.20 males (24.1%) and 5 females (29.4%) of the patients had severe anaemia. 24 males (28.9%) and 6 females (35.3%) had moderate anaemia.27 males (32.5%) and 5 females (29.4%) had mild anaemia.12 males and 1 female had normal Hb level. Normocytic Normochromic anaemia was more prevalent than other types of anaemias. 43.7 % of the anaemic patients revealed normocytic normochromic picture, followed by microcytic hypochromic (28.7%) and macrocytic(25.3%) while 2.3 % patients had dimorphic picture. 28 males (39.4%) and 10 females (62.5%) had normocytic normochromic anaemia.21 males (29.4%) and 4 females (25%) had microcytic hypochromic anaemia. 20 males (28.2%) and 2 females (12.5%) had macrocytic anemia. In this study, 14 patients were positive for HBsAg and 13 were positive for Anti HCV. All 20 males having macrocytic anaemia gave history of chronic alcoholism.

Keywords: Anaemia, Decompensated, chronic liver disease.

INTRODUCTION

Liver is the largest organ of the body & performs many vital roles. Liver is the major storage site for iron, vitamin B12 and folic acid. The liver is responsible for various haematological abnormalities due to its unique portal circulation and its synthetic (clotting factors, thrombopoietin) and immune functions. Chronic liver diseases are frequently associated with hematological abnormalities. Presence of anaemia is associated with poor prognosis in cirrhosis. Anaemia is the most common health problem in the world. Anemia of diverse etiology occurs in about 75% of patients with chronic liver disease [1].

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 [2].The biosynthetic pathways of blood coagulation factors II, VII, IX and X are within the hepatocyte and are dependent on vitamin K[3]. 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. Yang *et al.* [4] investigated the significance of erythropoietin in 67 patients with varying severity of cirrhosis and reported that plasma erythropoietin levels were significantly higher in cirrhotic patients than in controls. Folic acid and vitamin B12 deficiencies and iron deficeincy develop frequently inpatients with cirrhosis producing severe anaemia.

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. Alcohol, a common etiologic factor of chronic liver disease, is toxic to the bone marrow. Alcoholics often develop secondary malnutrition, a manifestation of which may be anemia caused by folic acid deficiency. In some patients, bone marrow failure and aplastic anemia develop after an episode of hepatitis. Anemia is also 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 [5].

Other factors which contribute to development of anaemia in chronic liver disease include-

- Direct toxic effect of alcohol on the bone marrow
- Inflammatory cytokines suppresing the bone marrow (chronic inflammation)
- Wilson's disease may be associated with a hemolytic anaemia in 1-12%. Hepatic necrosis leads to release of copper, which in turn has an oxidative action on RBC cell membrane phospholipids leading to their breakdown. These patients typically present as fulminant hepatic failure with hemolysis [6].
- Hypersplenism consequent to portal hypertension.Using 51Cr-labelled RBCs, Subiyah and Al-Hindawi [7] demonstrated a correlation between a decrease in RBC survival and splenomegaly related to portal hypertension. They also showed that splenectomy resulted in improved RBC survival.
- There is now evidence to support the increased morbidity and mortality associated with hypersplenism. Liangpunsakul *et al.* [8] reported that the presence of severe hypersplenism independently predicted the development of variceal bleeding and death.
- Autoimmune hemolytic anaemia seen in association with autoimmune hepatitis.
- Chronic hepatocellular diseases are usually associated with decreased hepatic synthesis of coagulation factors, thrombocytopenia, impaired platelet function, hyperfibrinolysis and DIC which predispose to increased bleeding tendancy.

Patients with chronic liver disease can present with acute decompensation due to various causes. The decompensation may take the form of any of the following complications:

- Oesophageal variceal bleed
- Ascites
- Spontaneous bacterial peritonitis
- Hepatic encephalopathy
- Hepatorenal syndrome
- Hepatocellular carcinoma

This paper provides an insight into anaemia that may complicate chronic liver diseases and the mechanisms responsible.This could help in early diagnosis of anaemia in decompensated chronic liver disease patients and could play a role in treatment of patients earlier and prevent morbidity and mortality.

Objective

To assess the prevalence and spectrum of anaemia in decompensated chronic liver disease patients.

MATERIALS AND METHODS

Study design

Cross-sectional descriptive

Study Population

The prevalence was conducted in B.P.S. Government Medical College and hospital for women, Sonepat Haryana. One hundred patients were selected in random for this study, from patients coming to department of general medicine OPD and ward patients.

Inclusion Criteria

- All liver disease patients whose symptoms and signs persist for more than six Months and having signs of decompensated liver disease like ascitis, Variceal bleeding and hepatic encephalopathy were included in the study.
- Alcoholic, post infective, metabolic causes of liver diseases were taken into consideration.

Exclusion Criteria

- Patients with known primary hepatocellular carcinoma or GI malignancies.
- Acute liver cell failure.

History and clinical examination

A detailed history was taken such as abdominal pain, abdominal distension, decreased urine output, hemoglobin levels, yellowish discoloration of urine and eyes, loss of appetite, loss of weight, early satiety and fever.

Investigations

Oral and written consent of the patients for the clinical examination and for the lab investigations was taken. After detailed history and thorough clinical examination, blood investigations such as liver function tests were carried out. Ultrasound abdomen was done for all the patients to look for sonographic findings of decompensated liver disease in form of coarse echotexture of liver, splenomegaly, portal vein diameter, asctis etc. Once the patients was confirmed as a case of decompensated chronic liver disease, then the patients would undergo other tests such as Hb, RBC count, RBC indices i.e. MCV(mean corpuscular volume), MCH(mean corpuscular hemoglobin) MCHC(mean corpuscular hemoglobin concentration). Reticulocyte count and peripheral smear examination was done to find the type of anaemia. HBsAg and Anti HCV antibodies tests were done to look for these viral infections.

RBC count

RBC count was done in neubauers chamber using hayems fluid or autoanalyser. Normal value is 4.5-5.5 million per cu mm.

Haemoglobin Estimation

Done by Sahlis method, based on the conversion of Hb to acid haematin or acid analyser
Normal values: Male 14-18g/dl
Female 12-16g/dl

Peripheral Smear for Blood Picture

Peripheral blood smear examination was done by following methods to identify the typing of anaemia -
Low power field microscope
High power field microscope
Oil immersion examination

RESULTS

Anaemia is a frequently observed manifestation during clinical course of chronic liver disease. In this study, 100 chronic liver disease patients (83 males and 17 females) were assessed for the frequency and typing of anaemia WHO fulfilled the criteria to be included in the study. The mean age of the patients was 44±14 years. The minimum and maximum ages of the patients included were 16 & 85 years respectively. The male/female ratio was 4.9/1.The mean Hb value was 9.5±1.92g/dl. The mean MCV was 89.2±11.02fl.

Grading of Anaemia was done according to WHO criteria:

- Grade 1, considered mild anaemia, is Hb from 10 g/dl to the lower limit of normal which is 13g/dl for males & 12 g/dl for females.
- Grade 2 anaemia or moderate anaemia is Hb from 8 to less than 10g/dl.
- Grade 3 or severe anaemia is below 8g/dl.

We found that 87% patients of decompensated chronic liver disease in our study were anaemic. In this study, 20 males (24.1%) and 5 females (29.4%) of the patients had severe anaemia. 24 males (28.9%) and 6 females (35.3%) had moderate anaemia.27 males (32.5%) and 5 females (29.4%) had mild anaemia.12 males and 1 female had normal Hb level. Female patients had a greater proportion of severe anaemia as compared to male patients in our study. Table 1 shows grades of anaemia in patients of decompensated chronic liver diseases.

Table-1: Gender distribution of grades of anaemia

	GENDER					
	MALE		FEMALE		TOTAL	
HAEMOGLOBIN (g/dl)	N	%	N	%	N	%
SEVERE (<8g/dl)	20	24.1	5	29.4	25	25
MODERATE (8-9.9 g/dl)	24	28.9	6	35.3	30	30
MILD (9-12.9g/dl)	27	32.5	5	29.4	32	32
NORMAL	12	14.5	1	5.9	13	13
TOTAL	83	100	17	100	100	100

In our study, Normocytic Normochromic anaemia was more prevalent than other types of anaemias.

43.7 % of the anaemic patients revealed normocytic normochromic picture on peripheral blood film examination, followed by microcytic hypochromic (28.7%) and macrocytic(25.3%) while 2.3 % patients had dimorphic picture. 28 males (39.4%) and 10 females (62.5%) had normocytic normochromic anaemia. Microcytic hypochromic anaemia was found more prevalent in men than women in this study.21 males (29.4%) and 4 females (25%) had microcytic hypochromic anaemia. 20 males (28.2%) and 2 females (12.5%) had macrocytic anaemia. In this study, 14 patients were positive for HBsAg and 13 were positive for Anti HCV.A total of 62 patients (all males) gave history of alcohol consumption. All 20 males having

macrocytic anaemia gave history of chronic alcoholism. A strong correlation was found between chronic alcohol consumption and macrocytic anaemia. 2 males (2.8%) had dimorphic anaemia. Target cells were also seen in about 2% patients in our study, 12 males and 1 female had normal Hb levels.

Table-2: Type of Anaemia in Chronic liver disease patients

	PATIENTS WITH ANAEMIA					
	MALE		FEMALE		TOTAL	
Types of rbc	N	%	N	%	N	%
Normocytic	28	39.4	10	62.5	38	43.7
Microcytic	21	29.6	4	25	25	28.7
Macrocytic	20	28.2	2	12.5	22	25.3
Dimorphic	2	2.8	0	0	2	2.3
Total	71	100	16	100	87	100

DISCUSSION

In the study, we inferred that 87% of the total patients had anaemia and among them 25% of cases had severe anaemia. Previous studies have shown that anaemia occurs in up to 75% of patients with chronic liver disease [1]. It is characteristically of moderate severity and is either normochromic normocytic (9, 10) or moderately macrocytic.

In our study 25 patients (25 %) had severe anaemia less than 8 gm per cent Hb.

Female patients had a greater proportion of severe anaemia when compared with males in our study. It shows the poor nutritional status of women in developing countries.

Characteristics of Anaemia

Anemia of diverse etiology occurs in about 75% of patients with chronic liver disease [1]

- According to previous studies, most common anaemia seen in cirrhotic patients is normochromic and normocytic anaemia [9, 10] It is well proven in our study too.
- A normocytic anemia is defined as an anemia with a mean corpuscular volume (MCV) of 80–100 which is the normal range. However, the hematocrit and hemoglobin is decreased.
- The incidence of normochromic normocytic anaemia in our patients is 43.7 %.
- In some studies such as Kimber C. *et al*. [11] reported 43% of macrocytosis. The incidence of macrocytosis in our patients was 25.3%
- Macrocytosis in cirrhosis is mostly due to the toxicity of alcohol on RBC production in the bone marrow and deficiency of B12 and folic acid [12].
- In our study, Macrocytic anaemia was found in 20 males all having history of chronic alcoholism for more than 8-10 years. Only 2 females had macrocytic picture and none of the females were alcoholic.
- Microcytosis in cirrhosis due to decreased total iron concentration with alterations in iron metabolism due to decreased serum transferrin and Hemolysis due to hypersplenism, autoimmune process, lipid abnormalities or intracorpuscular defects.
- Serum iron is bound to P globulin transferrin and total iron binding capacity largely depends on transferrin concentration. The TIBC is often lowered in cirrhosis due to reduced hepatic synthesis of transferrin.

CONCLUSIONS

In this study, 87 percent (n=87) of the patients had anaemia. Normocytic normochromic anaemia is most common type of anaemia present in our study in patients having decompensated chronic liver disease. Microcytic anaemia is more common in men than women in this study. Majority of Macrocytic anaemia patients gave history of Chronic Alcoholism.14 patients were positive for HBsAg and 13 were positive for Anti HCV.

In this study, 87 percent (n=87) patients had anaemia, which indicates that earlier diagnosis and intervention for Anaemia in decompensated chronic liver disease patients would help us to treat patients earlier and prevent morbidity and mortality

Our study revealed presence of anaemia in more than 3/4of the patients of decompensated chronic liver disease with 1/4 of them having severe anaemia, Normocytic anaemia being most prevalent in this study. Presence of anaemia in chronic liver disease patients significantly affects the quality of life. Detection of the underlying causes & timely intervention can help improve the prognosis.The occurrence anemia in patients with cirrhosis may have significant clinical implications.

Treatment of anaemia in cirrhosis involves a multifaceted approach. It includes transfusion of packed RBCs in those having severe anaemia, Iron, Vitamin B12 or folic acid supplementation depending upon the cause of anaemia. Prevention of bleeding with gastrointestinal prophylaxis using proton pump inhibitors, and transfusion of platelets before procedures may reduce the risk of bleeding with

accompanying thrombocytopenia. Advising patients for alcohol abstinence can prevent further worsening of anaemia. Timely diagnosis and management of chronic hepatitis B and Hepatitis C can cause significant reduction in morbidity and mortality.

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