ORIGINAL ARTICLE

RED BLOOD CELL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE (DCLD)

G. Anbazhagan[1], P. Mohan Raj[2], S. Kalaivalli[3], Vishnuprasanth[4]

HOW TO CITE THIS ARTICLE:
G. Anbazhagan, P. Mohan Raj, S. Kalaivalli, Vishnuprasanth. "Red Blood Cell Abnormalities in Decompensated Chronic Liver Disease (DCLD)". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 7, February 16, 2015; Page: 826-833.

ABSTRACT: BACKGROUND: Liver plays an important role in normal erythropoiesis, especially in formation and destruction of RBC's. Chronic liver diseases are frequently associated with hematological abnormalities. Anemia of diverge etiology occurs in about 75% patients with DCLD (36). This can ultimately culminate in grave complications. **AIM OF THE STUDY:** To detect various abnormalities in Red Blood Cells and to assess the type of anemia in DCLD. **METHODS:** The study was conducted in 50 patients of DCLD, in Meenakshi Medical College. A detailed History, clinical examination and also Ultrasound Abdomen, GI endoscopy to establish DCLD and complete Red Blood Cell assessment was done. **RESULTS AND OBSERVATION**: Among the 50 patients, 40 patients (80%) had anemia and only 10 pts had normal hemoglobin above 13 gms%. About 15 patients (30%) had severe Anemia of less than 6 gm%. Among the 40 patients, 25 patients had normocytic normochronic anemia, 10 patients had microcytic anemia, and 4 patients had macrocytosis and only one had dimorphic anemia. **CONCLUSION**: Most common Red Blood Cell abnormality in DCLD is anemia (80%) and most common anemia is normochronic normocytic anemia (62.5%), while microcytic anemia and macrocytosis were common among females and Alcoholics, respectively.

KEYWORDS: Cirrhosis of liver, Anemia.

INTRODUCTION: Liver plays important role in normal erythropoiesis especially in formation and destruction of Red blood cells. Chronic liver diseases frequently are associated with hematological abnormalities. Anemia of diverse etiology occurs in about 75% of patients with chronic liver disease.[1]

Chronic disease process of the liver involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.(2) Hepatocellular failure, portal hypertension and jaundice may affect the blood picture. Dietary deficiencies, alcoholism, bleeding and difficulties in hepatic synthesis of proteins used in blood formation or coagulation add to complexity of the problem.

Numerous hematologic manifestations of cirrhosis are present, including anaemia from a variety of causes including hypersplenism,(3) haemolysis, iron deficiency, and perhaps folate deficiency(4) from malnutrition.

Liver acts as a storage organ for vitamin B12 and folic acid which are necessary for the maturation of RBCS. Liver secretes transcobalamin I, which is necessary for the transport of B12 to the storage site. Liver also secretes transferrin which helps in the transport of iron from the site of absorption to bone marrow for the synthesis of heme and RBCs production.

The anaemia is also due to several other factors, including blood dilution secondary to increased plasma volume and splenic pooling of red cells, which can trap up to 25 per cent of the total circulating red cell mass, depending upon the size of the spleen. Red cell survival is also decreased, by up to 50 per cent, and this is also proportional to spleen size. Depending upon the underlying aetiology of the portal hypertension, there may be an added element of inadequate bone marrow response to anaemia.

AIM OF THE STUDY: Aim of the study is to detect various abnormalities in Red blood cells and to assess the type of anaemia in chronic decompensated liver disease.

MATERIALS AND METHODS: The prevalence study was conducted in Meenakshi Medical College and Hospital, Kanchipuram in 50 inpatients.

INCLUSION CRITERIA:

1. Alcoholic, post infective and metabolic causes of liver diseases were taken for study.
2. Patients whose symptoms and signs persist more than 6 months.

EXCLUSION CRITERIA:

1. Patients with known GIT malignancy or known primary hepatocellular carcinoma.
2. Patients with primary coagulation disorder.
3. Acute liver cell failure.
4. Liver cell failure due to septicaemia or endotoxemia other than primary liver causes.

A detailed past, personal, family history was taken and clinical examination was performed in all patients. Patients were evaluated for chronic liver disease to establish the diagnosis of cirrhosis. Diagnosis was established with ultrasound and ascetic fluid analysis. According to Schalm Sw. The diagnosis of cirrhosis J. Hepatol 1997; 27: 1118, ultrasound can pick up 87% of cirrhosis.

For further evidence portal gastropathy or varices in upper GI endoscopy was also done. Above investigations were also supported with clinical signs of liver cell failure, to establish diagnosis. After establishing the diagnosis patients were evaluated for red blood cell abnormalities.

TO ASSESS RBC ABNORMALITY: RBC count, Haemoglobin estimation, packed cell volume (PCV), Mean Corpuscular Volume, Mean Corpuscular Haemoglobin Concentration, Mean Corpuscular Haemoglobin was estimated by auto analyser. Peripheral smear for blood picture by wedge slide method. Using stains, blood picture is examined with a microscope. Reticulocyte count was done using 1% brilliant cresol blue stain.

RESULTS AND OBSERVATIONS: Out of 50 patients in this study, there are 44 male patients and 6 female patients. The ages of patients in this study were in the range from 20 to 70. Most of the patients in the study were in the middle age group and only 3 patients (6%) were in younger

age. Out of three patients, one patient was diagnosed to have Wilson's disease and others were of unknown aetiology. Remaining 47 patients were diagnosed as chronic decompensated liver disease with pathology as cirrhosis and were of variable aetiology.

Among 50 patients only 16 patients had past history of jaundice. Later serology investigation for HBV Ag, anti HCV antibody shows 6 patients were positive for HBS Ag and only one shows positive for anti HCV antibody.

Haemoglobin (gm/dl)	Male		Female		Total	
	N	%	N	%	N	%
Severe (<6gm/dl)	12	27.27%	3	50%	15	30%
Moderate (6 TO 8.9/dl)	14	31.81%	2	33.33%	16	32%
Mild (9 TO 12.9 gm/dl)	8	18.18%	1	16.66%	9	18%
Normal (>13gm/dl)	10	22.72%	0	0%	10	20%
Total	**44**	**100%**	**6**	**100%**	**50**	**100%**

Table 1: Anaemia in DCLD patients

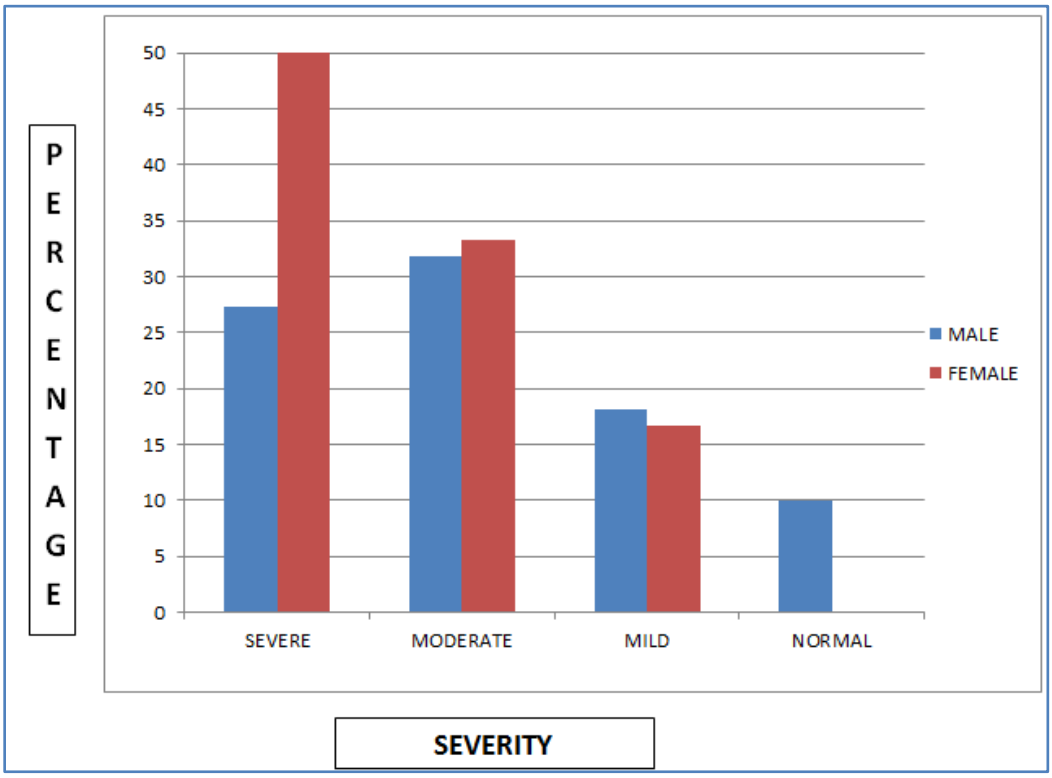

Figure 1

FIGURE 1: Patients in the study were analysed for the presence and absence of anaemia and the characteristics of anaemia when present. 40 patients (80%) had anaemia and only 10 patients (20%) had normal haemoglobin above 13 gm%. About 15 patients (30%) had severe anaemia less than 6 gm%.

Type of RBCs	Male		Female		Total	
	N	%	N	%	N	%
NORMOCYTIC	23	67.64%	2	33.33%	25	62.5%
MICROCYTIC	6	17.64%	4	66.66%	10	25%
MACROCYTIC	4	11.76%	0	0%	4	10%
DIMORPHIC	1	2.94%	0	0%	1	2.59%
Total	**34**	**100%**	**6**	**100%**	**40**	**100%**

Table 2: Type of anaemia in DCLD patients

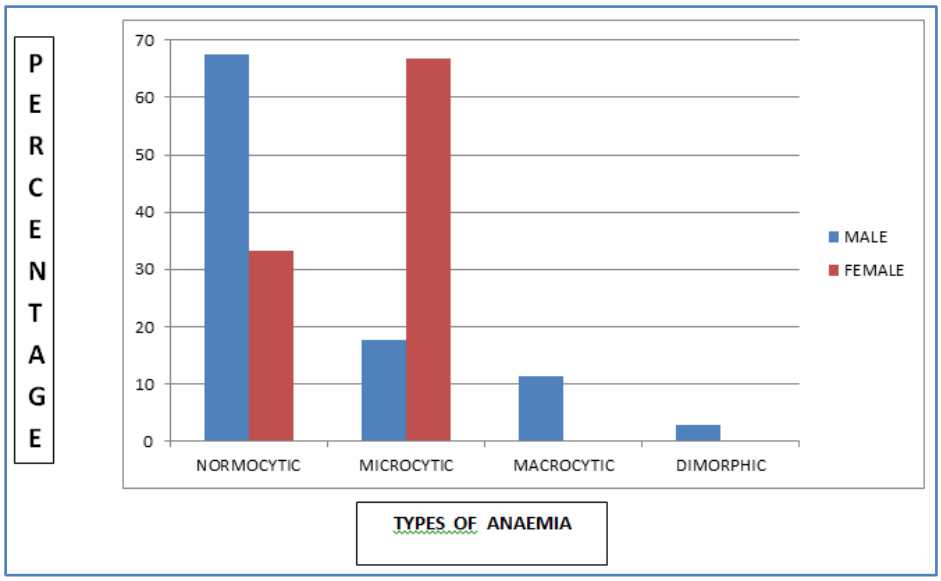

Figure 2

FIGURE 2: All the ten patients with normal haemoglobin level had normochromic and normocytic blood picture. Among the 40 anemic patients, 25 patients (62.5%) had normochromic and normocytic anemia, 10 patients (25%) had microcytic anemia and 4 patients (10%) had macrocytosis. Only one (2.5%) had dimorphic anaemia. Three patients with microcytic anemia showed anisocytosis and poikilocytosis. Target cells were seen in only one patient. Acanthocytes was not seen in any of the peripheral smears. Patients with macrocytosis had mean corpuscular volume more than 97 fl. Microcytic anaemia was seen more commonly in females (66%) than males (17.64%) in this study.

TYPE OF ANAEMIAs	ALCOHOLIC ANAEMICS (29 pts)			NON ALCOHOLIC ANAEMICS (11 pts)		
	M (29 pts)	F (0 pts)	TOTAL	M (5 pts)	F (6 pts)	TOTAL
NORMOCYTIC	21 (72.41%)	0	21 (72.41%)	2 (40%)	2 (33.33%)	4 (36.4%)

MICROCYTIC	4 (13.79%)	0	4 (13.79%)	2 (40%)	4 (66.6 %)	6 (54.5%)
MACROCYTIC	4 (13.79%)	0	4 (13.79%)	0	0	0
DIMORPHIC	0 (0%)	0	0 (0%)	1 (20%)	0	1 (9.1%)
TOTAL	29	0	29	5	6	11

Table 3: Pattern of anaemia in Alcholic & Non Alcoholic in DCLD patients

Among the 6 female patients, none gave history of alcoholism and among the 44 male patients 29 patients (65.9%) were found to be alcoholic. In this study, macrocytic anaemia was seen in 4 patients (13.8%) in alcoholic anaemic patient group (29 pts), whereas no patient was found to have macrocytic anaemia in non-alcoholic anaemic patient group.[5]

DISCUSSION: In the study we inferred that 80% of the total patients had anaemia and among them 30% of cases had severe anaemia.

According to studies by Kimber C, Deller DJ and Lander H.[6] The mechanism of anaemia in CLD 1965 and Sheehy W and Berman A,[7] the anaemia of cirrhosis, anaemia occurs in up to 75% of patients with chronic liver disease. It is characteristically of moderate severity and is either normochromic normocytic[8,9] or moderately macrocytic.

In our study 15 patients (30 %) had severe anaemia less than six gm per cent. In uncomplicated cirrhosis it is rare to have such low level of haemoglobin as anaemia in cirrhosis mostly due to:

1. Hemodilution.
2. Decreased erythropoietin level as per the study Siciliano Hepatol 1995[10] who showed decreased erythropoietin level in cirrhosis patients with anaemia when compared with patients with chronic anaemia due to iron deficiency. Cirrhosis without anaemia is not associated with low erythropoietin levels[11] (Piris , J Hepatol 1994).
3. Chronic inflammation in cirrhosis leads to increased levels of serum inflammatory cytokines which suppress the bone marrow.[12]

But severe anaemia in cirrhosis will necessitate the investigations to rule out the following conditions, Bleeding esophageal varices, Bleeding peptic ulcer, Malignancy, Haemolysis, Bleeding anorectal varices and Increased bleeding tendencies.

In developing countries like India, people with poor socio economic status will have nutritional anaemia due to iron deficiency and B12 and folic acid deficiency, which is superimposed with cirrhosis leading to severe anaemia. Female patients had a greater proportion of severe anaemia when compared with males. It shows the poor nutritional status of women in developing countries.

According to Sheila Sherlock[13] and Oxford text book of hepatology.[5] Most common anaemia seen in cirrhotic patients is normochromic and normocytic anaemia.[6][7] It is well proven in our study too. The incidence of normochromic normocytic anaemia in our patients is 62.5 %, where as in some studies there are varied results. According to study done by Malhotra, 1951,

the incidence was 90%. In studies done by Bhatia (1961) and Mishra et al., (1982), the incidences were 59% and 79% respectively.

In some studies such as Kimber C. et al.,[6] reported 43% of macrocytosis, which was supported also by the study by Bingham et al. The incidence of macrocytosis in our patients was 10%, 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.[14] Folic acid deficiency is also exacerbated with alcohol which was confirmed by the study done by Weir, Biochem. Pharm, 1985, and Lindenbaum.

About 10 patients in our group had microcytic hypochromic anaemia. Bleeding from esophagitis, peptic ulceration or esophaesophageal varices, compounded by the hemostatic defects of chronic liver disease, occurs in up to 70% of patients with Liver disease or per the study conducted by Kimber, Philips, et al., 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.[3]

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.

Target cells are also thin macrocytes are found in cholestatic jaundice and hepato cellular jaundice. They have increased resistance to osmotic lysis. They are particularly prominent in cholestasis where a rise in bile acids may contribute by inhibiting lecithin cholesterol acyl transferase (LCAT) activity[15] which was proved by the study conducted by Cooper RA, Arner EC. It is seen in 2% of patients in our study.

Spur cells or acanthocytes which are associated with advanced liver disease, are bad prognostic sign.[16] They are not found in our study groups. They form because of an interaction with the abnormal HDL found in Liver.[17]

CONCLUSION:

1. According to this study conducted with limited cases of 50 patients, we inferred many conclusive results regarding the Red Blood Cells abnormalities in decompensated chronic liver disease patients.
2. Almost 80% of the patients had anaemia in any one of the form.
3. Most common anaemia in cirrhosis is normochromic, normocytic anaemia as inferred from the study.
4. Microcytic anaemia is most common among women.
5. Macrocytosis is common with alcoholics.

REFERENCES:

1. McHutchison JG, Manns MP, Longo DL. Definition and Management of anemia in patients infected with hepatitis C virus. Liver Int. 2006; 26: 389-398. (PubMed)
2. Middle-East Journal of Scientific Research 7(6): 1001-1007,2011 ISSN 1990-9233© idosi publications, 2011.

3. Lindenbarum J, Lieber CS, Effects of chronic ethanol administration on intestinal absorption in man in the absence of nutritional deficiency. Ann. NY ACad. Sci, 1975, 252: 228-234.
4. Fergunson, J. Skikne, B.S, Simpson, K.M., Baynes, R.D & Cook J.D (1992).Serum transferrin receptor distinguishes the anemia of chronic disease from iron deficiency anemia. J.Lab. Clini. Med. 1992; 19: 385.
5. Haussinger D. In:Oxford text book of hepatology II edition, Bircher J, Benhamou J, McIntyre N, Rizzetto M, Rodes J, Eds, Oxford University Press, Oxford, 1999, pg 325.
6. Kimber C, Deller DJ, Ibbotson RH, and Lander H. The mechanism of anaemia in chronic liver disease. Quarterly Journal of Medicine, 1965; 34: 33-64.
7. Sheehy TW and Berman A. The anaemia of cirrhosis. Journal of Laboratory and Clinical Medicine, 1960; 56: 72-82.
8. Rubiee, CRY Med. 1977, 40: 338.
9. Schmidt K, Waever Rasmussen JDahl Rasmussen A, Arendrup H, Comparative studies of the in vivo kinetics of simultaneously injected 111in- and 51Cr-labelled human platelets. Sca J. Hematol, 1983. 30: 465-78.
10. Siciliano M, Tomasello D, Milani A, Ricerca BM, Storti S, Rossi L, Reduced serum levels of immuno reactive erythropoietin in patients with cirrhosis and chronic anemia, Hepatology, 1995, 22: 1132-5.
11. Piris M, Fabris C, Soardo G, CEcchin E, Toniutto P, Bartoli E, Thrombocytopenia of chronic liver disease corrected by erythropoietin treatment. J. Hepatol, 1994, 21: 376-80.
12. Berman I, Axelord AR, and Horan TN. The blood and bone marrow in patients with cirrhosis of the liver. Blood, 1949; 4: 511-33.
13. Sheila Sherlock. Disease of Liver, Biliary system 11th edition, 25 Oct 2007.
14. Means RT and Krantz S. Progress in understanding the pathogenesis of the anaemia of chronic disease. Blood, 1992; 80: 1639-47.
15. Carr JM. Disseminated intravascular coagulation in cirrhosis. Hepatology, 1989; 10: 103-10.
16. Lindenbaum J. Hematologic complications of alcohol abuse. Sem. Liver. Dis, 1987, 7: 169-181.
17. Phillips DL and Keeffe EB. Hematologic manifestations of gastrointestinal disease. Hematology/Oncology Clinics of North America, 1987; 1: 207-28.

AUTHORS:

1. G. Anbazhagan
2. P. Mohan Raj
3. S. Kalaivalli
4. Vishnuprasanth

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Medicine, Meenakshi Medical College & Research Institute, Kanchipuram.
2. Assistant Professor, Department of Medicine, Meenakshi Medical College & Research Institute, Kanchipuram.
3. Professor & HOD, Department of Medicine, Meenakshi Medical College & Research Institute, Kanchipuram.
4. Junior Resident, Department of Medicine, Meenakshi Medical College & Research Institute, Kanchipuram.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. G. Anbazhagan,
5/102, Karikacan Salai,
Sathiya Nagar, SIPCOT,
Ranipet, Vellore District,
Tamil Nadu-632403.
E-mail: anubuchithra@yahoo.co.in

Date of Submission: 22/01/2015.
Date of Peer Review: 23/01/2015.
Date of Acceptance: 30/01/2015.
Date of Publishing: 11/02/2015.