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A Study on Hematological Abnormalities in Patients with Chronic Liver Disease

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Abstract | **Original Research Article**

Abnormalities in hematological indices are frequently encountered in cirrhosis of liver. Multiple causes are contributing to the occurrence of hematological abnormalities. Recent studies suggest that the presence of hematological cytopenias is associated with a poor prognosis in cirrhosis. This study was conducted on 43 patients with chronic liver disease to assess the hematological abnormalities. We found 37(90%) patients had hemoglobin <12gm/dl. Macrocytic anemia was predominant type followed by normocytic normochromic and microcytic type. 24 patients had platelets <1.5lakh /dl. 28 patients had prolonged prothrombin time and INR was raised in 38 patients. 12 patients showed peripheral smear picture suggestive of pancytopenia. We observed patients with anemia had MELD score above 15% compared to patients without anemia. We also observed patients with MELD score above 20% had mean platelets of 1.5l/dl compared to lower score. 38 patients had splenomegaly. We also observed mean platelet count in patient with hepatic encephalopathy was low and prolonged prothrombin time.

Key words: Hematological spectrum in cirrhosis.

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, lipid metabolism, inactivation of various toxins, metabolism of drugs, hormones, and synthesis of plasma proteins & maintenance of immunity (Kupffer cells). Right from being a primary site of hematopoiesis in fetal life to maintenance of hematological parameters in postnatal life. The liver has an extremely important role in maintenance of blood homeostasis. It acts as a storage depot for Iron, Folic acid & Vitamin B12, Secretes various clotting factors and inhibitors. Hence it's not surprising to see a wide range of hematological abnormalities in liver diseases [1].

Decompensated chronic parenchymal liver disease is one of the most common diseases encountered in day to day practice. Because of chronic disease many hematological abnormalities are present in these patients. The hematological abnormalities in a chronic disease add morbidity to the primary pathology and increase the mortality. Hence it becomes necessary to investigate the hematological abnormalities and hemostatic abnormalities to decrease the co morbidity. Abnormalities in hematological parameters are common in patients with cirrhosis. The pathogenesis of abnormal hematological indices (HIs) in cirrhosis is multifactorial and includes portal hypertension-induced sequestration, alterations in bone marrow stimulating factors, viral- and toxin-induced bone marrow suppression and consumption or loss[2,3].

Abnormalities in HI s are associated with an increased risk of complications including bleeding and infection [4]. Various studies on patients with varying stages of cirrhosis have shown a prevalence of abnormal hematological abnormalities ranging from 6% to 77% [5, 6].

In a recent analysis of homogenous patients with compensated Child-Pugh class A/B cirrhosis, 84% were found to have abnormalities in the hematological indices (HI), defined as a platelet count of less than or equal to 150×109/L, WBC count of less than or equal to 400×109/L or hemoglobin level less than or equal to 135 g/L for men and 115 g/L for women. Thirty-two per cent of these patients had a combination of cytopenias[7]. Thrombocytopenia was the most common single abnormality and thrombocytopenia and leukopenia was the most common combined abnormality [8].

The study was conducted to at Raja Rajeswari Medical College and Hospital, Bangalore. The study was conducted to assess the hematological

abnormalities and dearrangements and the nature of hematological abnormalities mainly to reduce the morbidity. Broadly the hematological abnormalities are viewed under abnormalities in RBCs, WBCs, Platelets, coagulation profile.

MATERIALS AND METHODS

This study was conducted at RajaRajeswari Medical College and Hospital, Bangalore. Institutional Ethical committee clearance was obtained before the study. Informed consent was obtained from all patients who met with inclusion criteria.

Inclusion criteria

- Patients above 18 years
- Patients presenting with signs and symptoms of chronic liver disease
- Patients with ultrasound evidence of chronic liver disease with portal hypertension.

Exclusion Criteria

- patients with underlying malignancy or known primary hepatocellular carcinoma were excluded
- Patients with primary coagulation disorder or primary abnormalities of hemostatic function were excluded.
- Acute hepatic failure was excluded
- Patients with preexisting anemia due to other causes were excluded.
- Patients suffering from end stage medical diseases like COPD, Coronary artery disease, cardiac failure, CKD were excluded.

All patients who met with inclusion criteria were evaluated with detail history and clinical examination. Blood sample was taken for assessment of liver function tests, complete hemogram, coagulation profile, peripheral blood smear, ultrasound abdomen, renal function tests and baseline upper GI scopy was done for all patients. Results were analysed with statistics.

RESULTS

We conducted study on 43 patients with clinical and sonological diagnosis of chronic liver disease with various etiology. Hematological parameters including anemia, leukocyte count, prothrombin time and platelet count were assessed in the subjects and were categorized under the different groups of MELD score. The relationship of these variables with MELD score was studied and statistical analysis was done.

An observational non-interventional correlational clinical study. Maximum number of patients were between 41-50 years and 30-40 years. Only 6 patients were above 50years. 88% of patients were males and 12% were female. Alcohol consumption (38 patients), was common etiology for all these patients and 3 patients had cirrhosis of cryptogenic origin. 50% of patients had h/o alcohol consumption for more than 10 years. Ascites, jaundice, generalized weakness and edema of limbs for common symptoms at admission.

Table-1: Clinical investigations

Variables	No. of patients (n=41)	%
MCV		
• <80	3	7.3
• 80-95	15	36.6
• >95	23	56.1
Hemoglobin (g/dl)		
• ≤10	25	61.0
• 10-12	12	29.3
• 12-14	2	4.9
• >14	2	4.9
PS		
• MACROCYTIC	23	56.1
• MICROCYTIC	7	17.1
• NORMOCYTIC	11	26.8
Total count		
• <4000	13	31.7
• 4000-11000	20	48.8
• >11000	8	19.5
Platelets		
• <0.50	2	4.9
• 0.50-1.50	22	53.7
• >1.50	17	41.5
ESR		
• <35	11	26.8
• 35-60	26	63.4

• >60	4	9.8

Platelet count in study patients

• **<0.50**	2	4.9
• **0.50 – 1.50**	22	53.7
• **>1.50**	17	41.5

Table-2: Coagulation profile

	No of Patients(n=41)	**%**
PT, INR		
<20	13	31.7
20-40	27	65.9
>40	1	2.4
Raised INR		
< 3 sec	0	0.0
3 sec – 5 sec	22	53.7
> 5 sec	19	46.3

Table-3: Spleen size in patients studied

	No of Patients (n=41)	**%**
Spleen		
No	1	2.4
< 10	2	4.9
10-15	34	82.9
>15	4	9.8

Table-4: Meld score distribution of patients studied

MELD	**No of Patients**	**%**
1-9%	2	4.9
10-19%	11	26.8
20-29%	21	51.2
30-39%	7	17.1
Total	41	100.0

9 patients had bleeding manifestations. 37 patients had hemoglobin <12gm/dl, (table 1) macrocytic anemia was predominant type. 13 patients had leukopenia, 9 patients had leukocytosis and 20 patients had normal leukocyte count. Thrombocytopenia was observed in 24 patients. 30 patients had prolonged prothrombin time and INR (Table 2). Elevated total bilirubin was observed in 16 patients. 36 patients had serum albumin <3gm. Enlarged spleen of more than 10cm was observed in 38 patients (Table 3). We also observed peripheral smear suggestive of pancytopenia in 12 patients. We found 16 patients with upper GI evidence of varices. Most of patients with Platelets <1.5lakhs/dl had findings of upper GI bleed but only 2 patients with platelets above 1.5lakh had upper GI bleed. There was significant drop in hemoglobin and in platelets in patients with MELD score above 20%. Mean MCV was prolonged in patients with MELD score above 20%. This finding was statistically significant. In our study only 2 patients had MELD score <9%. Rest all patients had score above 20% and about 7 patients had score very high.

We also found there was increase in prothrombin time in patients who had MELD score above 15%. Mean duration of alcohol consumption was also >15 years in patients MELD score above 20%. There was significant rise in MELD score with fall in hemoglobin. Mean platelets was <1.5lakhs/dl in patients with MELD score above 15%. There observed mean low serum albumin and total protein among patients with high MELD score this observation was statistically significant (Table 5). Only 2 patients had MELD score <10 %. Rest all patients had high score. MELD score of above 30% was observed in 7 patients. We observed child‘s score of B in 19 patients and category C was seen in 7 patients. Most of the patients with high MELD score were presented with jaundice, ascites, and edema. Few patients had bleeding symptoms. There was significant correlation between high MELD score and hepatic encephalopathy in our patients.

Table-5: Comparison of clinical variables according to MELD score of patients studied

variabless	MELD				P value
	1-9%	10-19%	20-29%	30-39%	
Age in years	47.00±0.00	52.00±14.30	48.90±12.43	45.29±10.64	0.731
Duration	15.00±0.00	18.36±10.22	14.19±10.25	9.14±8.01	0.294
MCV	87.00±0.00	95.09±3.86	94.33±12.34	93.71±13.73	0.808
Hemoglobin (g/dl)	12.50±0.00	10.23±1.91	9.32±2.30	10.74±2.96	0.187
Total Count	5700.00±424.26	7514.55±5256.15	6200.00±3932.43	10500.00±6318.49	0.222
Platelets	2.63±0.33	1.72±0.95	1.52±0.87	1.59±1.07	0.440
ESR	42.50±17.68	48.64±13.42	46.09±14.49	48.43±16.83	0.948
PT INR	16.00±0.00	21.36±3.61	23.65±6.00	28.43±27.45	0.521
INR	1.11±0.01	1.69±0.48	1.95±0.57	2.51±2.52	0.348
TOTAL BILRUBIN	1.40±0.00	2.95±1.75	6.06±4.37	17.23±14.96	0.001**
OT	23.00±0.00	57.18±19.43	79.48±55.37	117.71±55.73	0.034*
PT	13.00±0.00	21.55±6.85	31.81±19.65	66.00±46.35	0.002**
TOTAL PROTEIN	8.20±0.00	6.36±0.84	6.15±0.74	6.03±0.85	0.008**
ALBUMIN	3.90±0.00	2.24±0.54	2.25±0.41	2.49±0.82	0.001**
SODIUM (mEq/l)	133.00±7.07	135.73±4.52	131.81±3.54	127.57±1.51	0.001**
POTASSIUM	4.60±0.00	4.27±0.45	4.05±0.52	3.81±0.54	0.142

DISCUSSION

The vital functions of many organs in the body depend directly or indirectly on the liver. The haemopoietic system is an exception. Beginning early in fetal life it excerts a profound influence on the formation and maintainence of blood. Though before birth it acts as a haemopoietic organ and after birth it plays an active and important role in the production of many elements necessary for homeostasis and haemotopoiesis. Indirectly, when the liver is damaged by either acute or chronic disease, the effect on these functions may be catastrophic. Liver plays a major role in carbohydrate, lipid and protein metabolism. Its role in hematological manifestations is important. Loss of Liver function can manifest as subtle metabolic abnormalities and derangements in hematological parameters which can ultimately culminate in grave complications. Liver plays a major role in maintaining the hematological parameters and maintain the homeostasis. Liver is the storage site for iron vitamin B12 and folic acid which are necessary for the normal hematopoiesis. Liver also secretes the clotting factors and inhibitors and keep the homeostasis in equilibrium. Chronic Liver disease is usually accompanied by hypersplenism. Diminished erythrocyte survival is frequent. Dietary deficiencies, alcoholism, bleeding and difficulties in hepatic synthesis of proteins used in blood formation or coagulation add to complexity of the problem. In our study we found anemia and thrombocytopenia are two major hematological abnormalities were observed. And presence of these abnormalities can affect prognosis of patients which was observed by elevated MELD score. And thus these abnormalities can contribute to patient's mortality. We also observed significant relation between prolonged prothrombin time and increase in MELD and child score. Once again presence of thrombocytopenia and prolonged prothrombin time can contribute to development of hepatic encephalopathy and adverse prognosis. We observed most of patients with thrombocytopenia and prolong PT had evidence of upper GI bleed and thus lead to development of hepatic encephalopathy and anemia [9, 10]. Hence identification treatment of all abnormal hematological indices are very vital part in management of patients with chronic liver disease [9]. Similar results are observed is previous studies by S. Selvamani *et al.* among the 100 patients 52 patients had normochromic and normocytic anemia, 30 patients had microcytic anemia and 16 patients had macrocytosis. Two had dimorphic anemia and thrombocytopenia was found in 46 patients[9]. Rajkumar Solomon T *et al.* in their study found 50 % of the patients had thrombocytopenia (<1 lakh), 13 patients who had an upper GI bleed 3 patients had normal platelet counts and the rest had counts below 1 lakh. He also found most of patients with thrombocytopenia had prolonged prothrombin time [1].

CONCLUSION

Apart from serum protein, albumin, which reflects synthetic function of liver, alteration in hematological parameters are telltale signs of chronicity of liver disease. Efforts can be made to normalize the hematological parameters so that we can reduce the mortality and morbidity of these patients effectively.

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