Section: Pathology

Original Research Article

STUDY OF HEMATOLOGICAL ABNORMALITIES AND BONE MARROW FINDINGS IN CHRONIC LIVER DISEASE IN A TEACHING HOPSITAL

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ABSTRACT

Background: Hematological abnormalities are common finding in Chronic Liver Disease(CLD). The liver keeps haematological parameters normal and preserves haemostasis by storing iron, vitamin B-12, and, folic acid, necessary for healthy haematopoiesis. Anaemia of various aetiologies affects approximately 75% of chronic liver disease (CLD) patients, specifically caused by iron deficiency, hypersplenism, chronic diseases, autoimmune haemolysis, folic acid deficiency, aplastic anemia. **Objectives:** To study Hematological abnormalities and Bone marrow findings Chronic Liver Disease patients.

Material and Methods: A cross sectional observation study done on 75 Chronic Liver Disease patients admitted in General medicine dept. At TRR medical college and Hospital for duration of 14 months i.e., from Feb 2021 to April 2023.

Results: Males were predominant accounting 66.6% and Females were about 33.3%. Mean age group among males was 53.14 years and females was 50.2 years. Alcoholic Liver Disease noted in 50.6% (38/75), Non-alcoholic Fatty Liver Disease and HBV in 13.3% (10/75). HCV in 12%(9/75),Primary biliary cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC) 4%(3/75) and Autoimmune hepatitis (AIH) 2.6% (2/75).MCH and MCV shows statistical significant correlation with p value 0.0089 and 0.04.WBC and Platelet also shows statistical significant correlation with p value <0.0001**** and 0.0092**.

Conclusion: One or More hematological abnormalities are noted in many Chronic Liver Disease(CLD) patients. Every CLD patient should be evaluated for hematological abnormalities and treated accordingly.

Key Words: Chronic liver disease, WBC, Platelets.

INTRODUCTION

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than 6 months, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile. CLD is a continuous process of inflammation, destruction, and regeneration of liver parenchyma, which leads to fibrosis and cirrhosis.[1]

Chronic liver disease is fourth leading cause of mortality among adults all over the world and is a pathogenic process of the liver characterized by progressive destruction and regeneration of parenchyma of liver causing fibrosis and cirrhosis.[1] The risk factors for CLD may vary in different populations. In developed countries, common risk factors are alcohol, chronic hepatitis B, chronic hepatitis C, and NASH, while in developing countries, predominant causes of cirrhosis are alcoholic, hepatitis B, hepatitis C, malnutrition, toxins, and some tropical infections are common.

Liver is the largest organ which is involved in metabolism. Liver is an important site for erythropoiesis and synthesis of procoagulant as well as anticoagulant proteins.[2,3] It is also a site for

storage of vitamin B12, iron and folic acid.[4] Chronic liver disease irrespective of etiology is associated with hematological abnormalities and since liver is the major site for erythropoiesis, anemia of various etiologies is also one of the common finding, which can be observed in as high as three fourth cases.[5]

Anemia in chronic liver disease occurs in 75% of patients with chronic liver disease.[6,7] It is mostly of moderate severity and is either normochromic normocytic or moderately macrocytic in uncomplicated cirrhosis36. If cirrhosis is complicated with hemorrhage or hemolysis then microcytic hypochromic anemia can occur.

Anemia in uncomplicated cirrhosis,[8,9,10] is due to :

1. Hemodilution - due to increased plasma volume.
2. Shortened red cell survival-hypersplenism.[11,12]
3. Reduced bone marrow response to anemia due to reduced erythropoietin level, chronic inflammation and increased level of inflammatory cytokines suppress the bone marrow,[13]

Leucopenia seen in CLD is due to hypersplenism or a toxic effect on bone marrow (alcohol). In neutrophil function there is a disturbance in late maturation compartment of granulocyte differentiation. Chemotaxis is inhibited. There is a low level of complement C3.[14,15,16]

Defects of platelet number and function are well documented in patients with CLD, contributing significantly to their hemostatic abnormalities.[17,18,19,20]

The mechanism for thrombocytopenia,[21,22,23] are:

1. Shortened mean platelet life span
2. Platelet pooling in an enlarged spleen
3. Inability of marrow to compensate
4. Reduced thrombopoietin production

Aim of The Study: To study hematological abnormalities and Bone marrow findings in chronic liver disease patients.

Its objectives

1. To assess the hematological abnormalities in a chronic liver disease patient.

a. To detect the abnormalities in RBCs
b. To find the type of anemia
c. To assess the WBC abnormalities.
d. To detect the Platelet abnormalities.
e. E. To asses bone marrow findings in CLD.

MATERIALS AND METHODS

Ethical permission was taken from Institutional ethical committee. Written consent was obtained from all the study participants.

This is a cross sectional observational study done on 75 patients with chronic liver disease in the department of General medicine at TRR medical college for duration of 14 months i.e. Feb 2021 to April 2023.

Inclusion Criteria

- Age more then18 years to 70 years
- Patients with chronic liver disease all confirmed by clinical findings, Coagulation profile, biochemical findings like LFT s and radiological evaluation including USG.

Exclusion Criteria

- Age less than 18 years.
- Patient on drugs which cause defect in haematological parameters (such as glucocorticoid, synthetic estrogen, aspirin, tamoxifen, methotrexate, OCP),
- Patients with malignancy.
- Pregnancy.

Methodology

- A detailed history was elicited from all patients with emphasis on symptomatology and history of presenting & past illness; personal & family history; drug & addiction history is taken. Detailed clinical evaluation including history including questioning about risk factors for chronic liver disease, history of hepatitis, alcohol consumption, diabetes melitus, transfusions, family history of liver disease, travel, and the presence of autoimmune diseases (including inflammatory bowel disease, rheumatoid arthritis and thyroid disease).
- All patients were then subjected to investigations such as routine hemogram, liver function tests, renal function tests, Peripheral smear examination and Bone marrow examination.

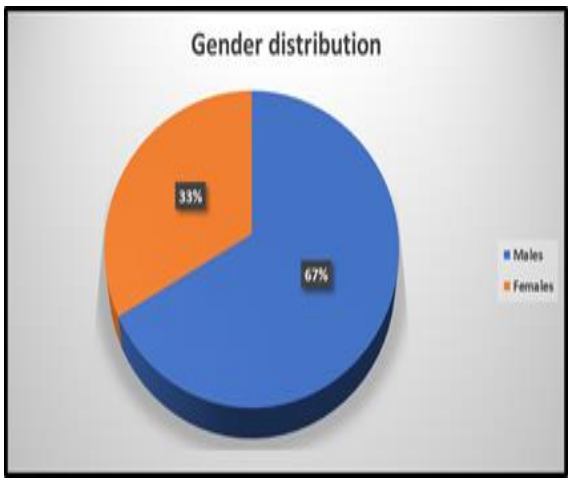
Statistical Methods

Data was compiled using MS Excel and analyzed with the help of statistical software namely SPSS 22.0. Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale .and chi square test has been used to analyse the data having ordinal variables. A p value of <0.05 was considered as significant.

RESULTS

In the present study age distribution varied from more than 18 years to 70 years. Majority were noted among 51-60 years constituting 36% and next common was among 41 -50 years accounting 29.3%. Mean age +SD- 52.15+2.5 Years.

According to Gender distribution: Males were predominant accounting 66.6% (50/75) and Females were about 33.3% (25/75). [Table 1]



Graph 1: Pie diagram showing gender distribution

According to Personal history: 53.3% (40/75) had history of Alcohol intake and 46.6% (35/75) were non Alcoholic.

According to distribution of clinical symptoms :Generalized weakness noted in 54.6% (41/75) cases, fever in 74.6% (56/75).

According to distribution of Past history : HbsAg in 8% (6/75), HCV 5.3% (4/75)

DM 17.3% (13/75), HTN 5.3% (4/75), DM/HTN 2.6% (2/75), Autoimmune hepatitis, ALD, Post liver transplant, 1.3%(1/75),CLD,ALD, Pancreatitis, 2.6% (2/75).

In our study Alcoholic Liver Disease noted in 50.6% (38/75), Non-alcoholic Fatty Liver Disease and HBV in 13.3% (10/75). HCV in 12%(9/75),Primary biliary cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC) 4%(3/75) and Autoimmune hepatitis (AIH) 2.6% (2/75). [Table 3]

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On lab investigations

In our study mild anemia (8.1 to 10 g/dl) were noted in 18.6% (14/75) cases ,

Moderate anemia (6.1 to 8 g/dl) in 17.3% (13/75) cases and severe anemia (<6 gm/dl) in 10.6% (08/75) cases and >10gm/dl in 53.3% (40/75) cases.

TLC between 2000-4000/cumm noted in 64% (48/75) cases,4000-11000/cumm in 26.6% (20/75) cases and <2000/cumm in 9.3% cases (07/75).

Platelet count between 1.4 to 4.4 lakhs /cumm (Normal) in 53.3% (40/75) cases,50000 to 1.3 lakhs(Mild Thrombocytopenia) in 14.6% (11/75),< 20000 /cumm(Severe thrombocytopenia) in 12% (09/75) ,Moderate thrombocytopenia in 13.3% (10/75),and > 4.4 lakhs/cumm in 13.3% (10/75).

On Peripheral smear examination findings: Normocytic Normochromic anemia noted in 54.6%(41/75), Macrocytic anemia in 18.6% (14/75) ,Microcytic Hypochromic anemia in 17.3%(13/75) ,Aplastic anemia 9.3% (7/75).

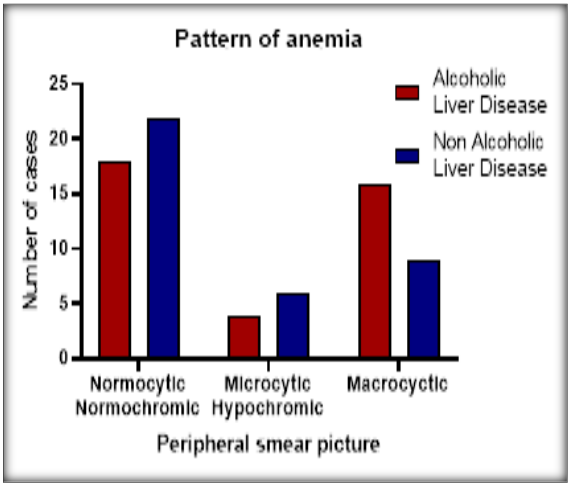
According to distribution of RBC indices :MCV,MCH and MCHC Decreased in 21.3% (16/75) cases .MCV,MCH Increased 25.3% (19/75) cases, normal MCV,MCH noted in 53.3% (40/75) cases and normal MCHC in 66.6% (50/75).

In our study Bone marrow Aspiration was done in only 30 cases and noted micro normoblastic marrow with decreased iron stores in 18.6% (14/75) cases, Megaloblastic anemia in 12% cases. And 3 cases MDS and Dry tap in 4 cases.

According to distribution of LFT findings: Total Bilirubin raised in 100% cases (75/75) and Raised SGOT and SGPT in 45.3% (34/75) cases.

In our study macrocytic anemia was more common in Alcoholic liver disease and microcytic hypochromic anemia was common in Non-alcoholic liver disease .

And does not show statistical significance on comparing Peripheral smear findings between Alcoholic and Non-alcoholic liver disease. [Table 4]



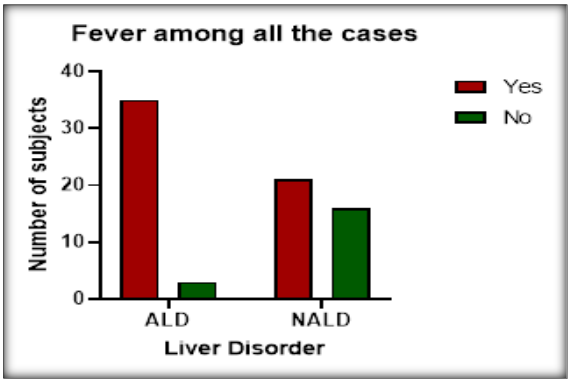
Graph 2: Bar diagram showing correlation of Peripheral smear examination between Alcoholic liver disease and non-alcoholic liver disease

In our study on Comparison of haematological parameters in Alcoholic liver disease and non-alcoholic liver disease - MCH and MCV shows statistical significant correlation with p value 0.0089 and 0.04.

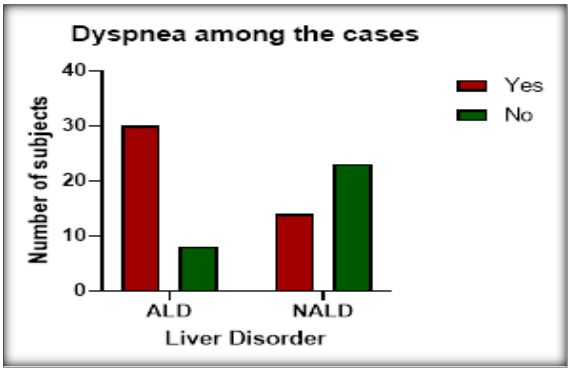
WBC and Platelet also shows statistical significant correlation with p value <0.0001**** and 0.0092**. [Table 5]

In our study SGOT and SGPT shows statistical significant correlation between Alcoholic liver disease and non-alcoholic liver disease. [Table 6]

In our study fever , dyspnoeas and Encephalopathy shows statistical significance correlation between Alcoholic Liver disease and non-alcoholic Liver disease. [Table 6]



Graph 3: Bar diagram showing correlation of clinical symptoms between Alcoholic liver disease and non-alcoholic liver disease



Graph 4: Bar diagram showing correlation of clinical symptoms between Alcoholic liver disease and non-alcoholic liver disease

Table 1: Age Distribution

Age distribution	No. of cases	Percentage
18 – 30 years	3	4
31 - 40 years	10	13.3
41 -50 years	**22**	**29.3**
51-60 years	**27**	**36**
61-70 years	12	16
>70 years	01	1.3
TOTAL	75	99.9%

Table 2: Distribution Based on Symptoms & Signs

SYMPTOMS	Present	Absent
Generalized weakness	41(54.6%)	34 (45.3 %)
Fever	56(74.6 %)	19 (25.3 %)
Dyspnea	44(58.6 %)	31(41.3 %)
Abdominal distension	40(53.3%)	35(46.6%)
Hematemesis /melaena	52(69.3 %)	23(30.6%)
Bleeding manifestations	57(76 %)	18(24 %)
Abdominal pain	66(88%)	09(12%)
Encephalopathy	12(16%)	63(84%)
Pallor	31(41.3 %)	44(58.6 %)
Icterus	31(41.3 %)	44(58.6 %)
Loss of body hair	30(40 %)	45(60%)
koilonychia	64(85.3 %)	11(14.6%)

Table 3: Distribution Based On Clinical Diagnosis

Etiology	No. of cases	Percentage
Alcoholic Liver Disease	38	50.6
Non-alcoholic Fatty Liver Disease	10	13.3
Chronic Viral Hepatitis		
HBV	10	13.3
HCV	9	12.2
Autoimmune Causes		
Primary biliary cirrhosis (PBC)	3	4
Primary Sclerosing Cholangitis (PSC)	3	4
Autoimmune hepatitis (AIH)	2	2.6
Total	**75**	**100%**

Table 4: Comparison of Pattern of anaemia in alcoholic liver disease and non-alcoholic liver disease(LD)

Peripheral smear findings	Alcoholic LD	Non Alcoholic LD	Total	p Value
Normocytic Normochromic	18	22	40	0.2532 ns
Microcytic Hypochromic	4	6	10	
Macrocytic	16	9	25	
Total	38	37	75	

Chi-square test, P <0.05 = significant, ns=not significant

Table 5: Comparison of haematological parameters in Alcoholic liver disease and non-alcoholic liver disease

Parameters	Alcoholic LD	Non Alcoholic LD	p Value
	Mean ± SD	Mean ± SD	
MCH	31.76 ± 6.339	28.16 ± 6.731	0.0089**
MCHC	35.00 ± 2.278	33.86 ± 2.710	0.0475*
MCV	105 ± 15.77	81.38 ± 17.23	0.0046**
HB	10.54 ± 2.879	10.95 ± 3.754	0.4805 ns
RBC	3.413 ± 0.2133	3.462 ± 0.3722	0.7688 ns
WBC	2916 ± 778.6	5154 ± 2456	<0.0001****
Platelet	214526 ± 176766	294838 ± 167370	0.0092**

Table 6: Comparison of Biochemical parameters in Alcoholic liver disease and non-alcoholic liver disease

Parameters	Alcoholic LD	Non Alcoholic LD	p Value
	Mean ± SD	Mean ± SD	
Total Bilirubin	2.645 ± 0.7493	2.470 ± 0.7280	0.2933
SGOT	49.55 ± 8.589	36.81 ± 7.352	<0.0001****
SGPT	65.03 ± 10.99	39.42 ± 11.44	<0.0001****

Mann Whitney test, P <0.05, * = significant, ns=not significant

Table 7: Symptoms among all cases of Alcoholic LD and non-alcoholic LD

Parameters	Alcoholic LD (38)		Non-Alcoholic LD(37)		p Value
	Yes (n)	No (n)	Yes (n)	No (n)	
Fever	**35**	**3**	**21**	**16**	**0.0005 *****
Dyspnea	**30**	**8**	**14**	**23**	**0.0004 *****
Abd Distention	20	18	20	17	>0.9999 ns
Hematemesis/ Malena	26	12	26	11	>0.9999 ns
Bleeding	30	8	27	10	0.5970 ns
Abd Pain	35	3	31	6	0.3091 ns
Encephalopathy	**11**	**27**	**1**	**36**	**0.0031 ** **
Pallor	17	21	14	23	0.6410 ns
Icterus	17	21	14	23	0.6410 ns
koilonychia	30	8	27	10	0.5970 ns

Fisher's exact test, P <0.05, * = significant, ns=not significant

DISCUSSION

Hematological abnormalities are common in patients with chronic liver disease and various factors have been observed to be associated with hematological abnormalities in CLD patients.[24] Our study aimed to assess the hematological abnormalities in CLD patients and to observed their association with severity and types of liver diseases.

Peripheral blood cytopenias are frequently observed in patients with chronic liver disease independent of etiology. The frequency and severity of cytopenia and the number of affected lineages increase with the progression of liver diseases. Thrombocytopenia develops first and may contribute to disease morbidity by increasing the risk of bleeding, followed by leukopenia and anemia.[25]

However, peripheral blood cytopenias may also develop due to bone marrow pathologies arising from primary hematological diseases unrelated to liver cirrhosis, such as myelodysplastic syndrome (MDS), newly onset leukemia, or bone marrow involvement in other primarily extramedullary diseases.

In the present study age distribution varied from more than 18 years to 70 years .Majority were noted among 51-60 years constituting 36% and next common was among 41 -50 years accounting 29.3% .Mean age 52.4 ± 2.19 . Similar findings were noted in Mukesh et al 26study with majority of patients belonged to 51 to 60 years of age (48%). with Mean age of 48.8±16.9 years . In Varun et al,[27] and In Deepika et al study,[28] mean age of 42.4 ± 8.19 years &48.23 ± 12.15 years respectively.

In our study males were predominant accounting 66.6% (50/75) and Females were about 33.3% (25/75). Similar findings were noted in Jasmine et al,[29] Deepika et al,[28] and in mukesh et al,[26] study with males constituting 86.6 %, 11.4 %,, 88% ,76% respectively.

In our study Generalized weakness was most common and noted in 54.6% cases, fever in 74.6% In Jasmine et al study 29 Abdominal distention (92.8 %) and fatigue (88.8 %) were the most common presenting symptoms. In Varun et al study 27Alcoholic liver disease was the underlying etiology of CLD in 30%, hepatitis B in 25% and hepatitis C in 20%. cryptogenic liver cirrhosis (17%), autoimmune liver disease (7%) and Wilson's disease (2%). In Mukesh et al study 26abdominal distension (71%). Hematemesis and Malena were noted in 15% and 12% cases respectively. About 3% cases had altered sensorium.

In our study Alcoholic Liver Disease noted in 50.6% (38/75) ,Non-alcoholic Fatty Liver Disease and HBV in 13.3% (10/75).HCV in 12%(9/75),Primary biliary cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC) 4%(3/75) and Autoimmune hepatitis (AIH) 2.6% (2/75).In Jasmine et al study,[29] Alcohol was the most common aetiology of cirrhosis in 52 patients (57.8 %), followed by hepatitis C in 16 patients (17.8 %), both alcohol and hepatitis C virus (HCV) in 10

patients (11.1%), Hepatitis B in 6 patients (6.6 %), other aetiologies in 6 patients (6.6 %).

In the present study mean Hb level was 10.7 g/dl. Mild anemia noted in 18.6% (14/75) cases, Moderate anemia in 17.3% (13/75) cases and severe anemia in 10.6% (08/75) cases .Leukopenia with TLC between 2000-4000/cumm noted in 64% cases and less than 2000/cumm in 9.3% cases. In our study, Mild Thrombocytopenia in 14.6% , Severe thrombocytopenia in 12% and Moderate thrombocytopenia in 13.3% and this could be associated with reduced levels of thrombopoietin in CLD, splenic sequestration, consumptive coagulopathy and bone marrow suppression.[30]

Our study findings were concordant with the findings of In Mukesh et al,[26] study anemia was observed in 71% cases whereas leukocytopenia and thrombocytopenia were noted in 21% and 56% cases respectively. and In a study done by Jasmine et al,[29] mean Hb level was 8.8 g/dl. 12 patients were having Hb in the normal range (13.3 %), 10 patients had mild anaemia (11.1 %), 29 patients had moderate anaemia (32.2 %) and 39 patients had severe anaemia (43.3 %). In Varun et al study,[27] the mean hemoglobin level was 8.7 gm/dl, 10% of the patients had platelet count 200,000 /cumm

In the present study Peripheral smear examination revealed Normocytic Normochromic anaemia as predominant form of anemia 54.6% followed by Macrocytic anemia in 18.6% and ,Microcytic Hypochromic anemia in 17.3%.Similar findings were reported by In Deepika et al,[28] Kumar et al,[31] and Jha et al,[1] study where they also noted Normocytic normochromic with Thrombocytopenia in CLD cases .Whereas in a study by Mukesh et al,[26] About 25% cases had microcytic normochromic anemia. Incidence of microcytic anemia was higher in NALD cases.

We also observed that the incidence of normocytic normochromic anaemia was common CLD but in alcoholic CLD, Macrocytic anemia was higher than non-alcoholic.

In our study, mean MCV and MCH were significantly higher in alcoholic CLD cases as compared to non-alcoholic cases, which could be attributed to folic acid and other

vitamin deficiency in alcoholic CLD, Similar findings were noted in mukesh et al,[27] study, Das et al,[32] and Tanriverdi et al.[33]

CONCLUSION

Hematological abnormalities particularly normocytic normochromic anemia and thrombocytopenia are common in cases with CLD, which might affect the prognosis of patients with CLD. Assessing the severity and type of anaemia is a useful tool for early initiation of the treatment in patients of CLD for reducing the morbidity and mortality. Early detection and treatment of haematological changes can prevent complications and reduce the mortality in CLD patients.

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