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TO STUDY HEMATOLOGICAL PROFILE IN CHRONIC LIVER DISEASE AND THEIR CORRELATION WITH SEVERITY OF THE DISEASES

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INTRODUCTION

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. Patients who have cirrhosis have varying degrees of compensated liver function, and clinicians need to differentiate between those who have stable, compensated cirrhosis and those who have decompensated cirrhosis. The Child-Pugh score is a reasonably reliable predictor of survival in many liver diseases and predicts the likelihood of major complications of cirrhosis such as bleeding from varices and spontaneous bacterial peritonitis.

Child-Pugh Classification of cirrhosis.[1]

Factor	Units	1	2	3
Serum bilirubin	mol/L mg/dL	<34 <2.0	34-51 2.0-3.0	>51 >3.0
Serum albumin	g/L g/dL	>35 >3.5	30-35 3.0-3.5	<30 <3.0
Prothrombin time	Seconds Prolonged INR	0-4 <1.7	4-6 1.7-2.3	>6 >2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

Note: The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Class A (5-6), B (7-9), C (10 or above).

Pathogenesis of hematological changes is multifactorial and included portal hypertension induce sequestration, alteration in bone marrow stimulating factors, viral and toxin induced bone marrow suppression and consumption or loss. Abnormalities in hematological indices are associated with increased risk of complications including bleeding & infection. Hence, by this study the correlation between abnormalities in hematological indices with severity of chronic liver disease can be revealed and future complications can be prevented by taking early steps.

AIMS AND OBJECTIVES

1. To evaluate various hematological indices in patients with liver cirrhosis & its correlation with severity of disease.
2. To assess platelet level specifically in relation to severity in chronic liver disease.
3. To study correlation of serum ferritin, vitamin B-12 level & Folic acid level with the severity of diseases.

MATERIAL AND METHODS

This study carried out in post graduate department of medicine, S.N. Medical College and hospital, Agra.

Study population: All diagnosed cases of chronic liver disease admitted in wards of Medicine department at S.N. Medical College, Agra.

Study duration: The study occurred within a period of one year.

Study Design: A hospital based cross sectional observational study.

INCLUSION CRITERIA

Previously diagnosed chronic liver disease patients and newly diagnosed patients admitted in wards during the duration of the study.

EXCLUSION CRITERIA

1. Patients previously diagnosed to have one of the following cause of chronic liver disease
   - Hemochromatosis
   - Primary biliary cirrhosis
   - Wilson's disease
   - Primary sclerosing cholangitis
2. Patients of chronic liver disease presenting with associated comorbid diseases like CRF, CHF
3. Anaemic patients already taking medications before being diagnosed as CLD.

INVESTIGATIONS

Each subject instructed to have following investigations:

- USG ABDOMEN
- CBC with GBP
- Liver function tests
  SGOT / SGPT S.Albumin
  S. Bilirubin Prothombin time
- S. Ferritin level
- S. vitamin B12 level
- S. folic acid level

Automated counter was used for Platelet count, hematological indices like MCV, MCH and MCHC. For haemoglobin level, cyanmethemoglobin method was used and for serum ferritin level, Serum vitamin b12 level & serum folic acid level by electro chemoluminenscence immune assay.

METHODOLOGY

STEP 1: Chronic liver disease pts who were previously diagnosed or diagnosed in wards was selected carefully using criteria laid down. Their written consent was taken. The history was elicited, physical examination & investigations were done.

STEP 2: From above blood reports and physical examination CHILD PUGH SCORING was done to assess the severity of the liver disease and classified in to Class A, B & C.

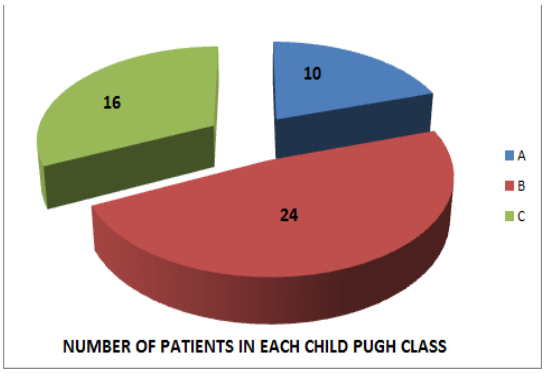
STEP 3: all selected patients was then categorised into three groups according to their CHILD PUGH CLASS.

Laboratory reports (Hb, platelet count, RBC indices, ferritin level, s. vit B12 level & s. folic acid level) of each patient, placed in each category was viewed thoroughly, to see any correlation of each lab report with increasing severity of chronic liver disease as per Child Pugh score.

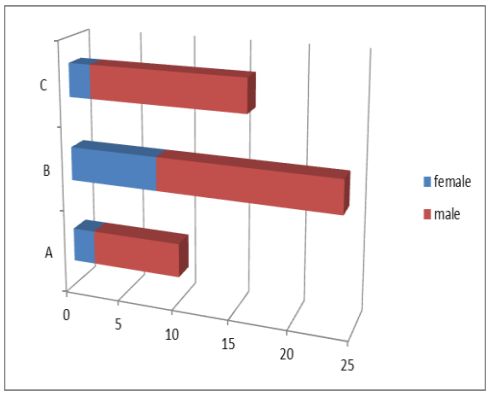
RESULTS

In this study, 50 CLD patients were taken, out of which 12 were female and 38 were male.

After applying Child Pugh score, three groups were made according to the C.P. class -. A, B & C.



Pie chart showing the division of patients into groups A, B & C according to Child Pugh Class.



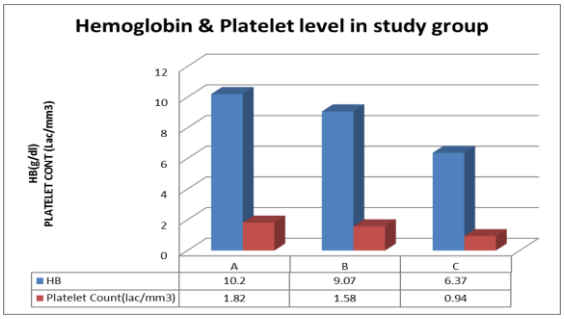
Distribution of selected patients in group A, B, C according to their Child Pugh Class.

Different hematological indices were studied to see their correlation with the increasing severity of the disease**.**

Hemoglobin level & Platelet level in study group.

In this study, it has been observed that as the severity of the disease increases, the hemoglobin level reduces. Mean hemoglobin level in group A found to be 10.2 ± 1.26 g/dl; in group B 9.07 ± 1.01g/dl; and in group C 6.37 ± 1.12g/dl (p=0.00).

The platelet count was normal in early stages but decreasing trend of platelet count was observed as the severity of CLD increases. The mean platelet count in group A was found to be 1.82 ± 0.443 lac/mm3; in group B 1.582 ± 0.404 lac/mm3 and in group C 0.948 ± 0.183 lac/mm3 (p=0.00).

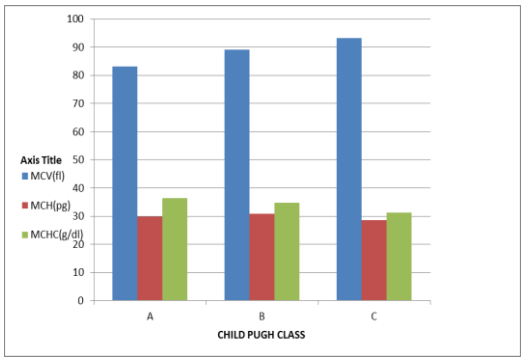


Bar diagram showing mean haemoglobin level & Platelet level in the study group.

MCV, MCH, MCHC level in the study group

The MCV level was showing increase with increase in severity of the disease with mean MCV level in group A is 83.05 ± 7.60 fl, in group B is 89.10 ± 6.99 fl, and in group C is 93.18 ± 8.02 fl (p=0.005).

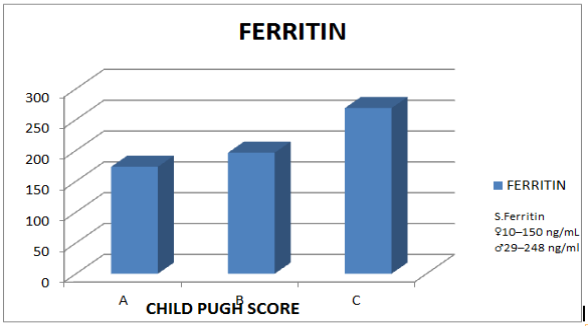
The MCH level & MCHC level showed a statistically insignificant change with mean MCH level in group A is 29.83 ± 1.69 pg, in group B is 30.80 ± 2.90 pg and in group C is 28.68 ± 6.63 pg (p=0.32) & mean MCHC level in group A 36.34 ± 5.40 g/dl, in group B 34.81 ± 4.68 g/dl, and in group C 31.27 ± 8.97 g/dl (p=0.113).



Bar diagram showing MCV, MCH, MCHC level in the study population

Serum ferritin level in the study group

We observed that as the disease severity increase, level of serum ferritin increases. The mean ferritin level in group A is 184.00 ± 66.87 ng/ml, in group B is 196.25 ± 60.69 ng/ml And in group C is 267.20 ± 54.81ng/ml (p=0.001).

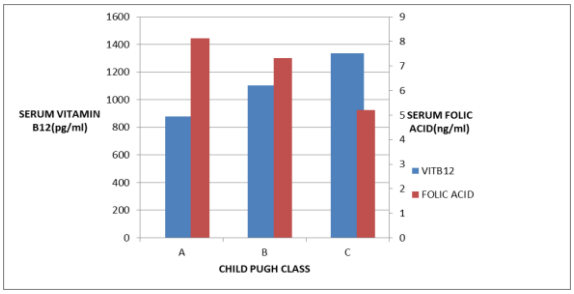


Bar diagram showing mean serum ferritin level in the study group.

Serum Vitamin B12 & Serum Folic Acid level in the study group

In this study, it has been observed that serum vitamin B12 level increases as disease severity increases. The mean vitamin B 12 level in group A 877.82 ± 314 pg/ml, in group B 1104.58 ± 145.013 pg/ml and in group C 1338.00 ± 277.271 pg/ml (p=0.00).

The serum folic acid showed statistically insignificant change with severity of the disease. The mean value of serum folic acid in group A is 8.12 ± 3.60 ng/mL, in group B is 7.33 ± 3.99 ng/ml, and in group C is 5.21 ± 1.75 ng/ml (p=0.73).



Bar diagram showing mean serum vitamin B12 & Folic acid level in the study population.

DISCUSSION

In this study, anemia aggravates as the disease severity increases, the Mean haemoglobin level in Child Pugh group A found to be 10.2 ± 1.26 g/dl; in group B 9.07 ± 1.01g/dl; and in group C 6.37 ± 1.12g/dl (p = .00). The study done by **Shivam Khare, et al**[2] over 100 CLD patients also showed same result. In alcoholic CLD cases, Child Pugh Class C patients were significantly higher in number with haemoglobin less than 8. (P= 0.005). In overall patients, Child Pugh class C cases had significant low haemoglobin in comparison to rest of group (p = 0.006).

Similar result was with the study conducted by **Qamar**[3] **et al** wherein, among 213 subjects, anemia was present in 126 subjects during the study, among which 37% had it at baseline, whereas 63% developed it during the course of the study. The most common anemia seen in cirrhotic patients is normochromic and normocytic anemia which is due to variceal bleeding, bone marrow suppression, hypersplenism etc and macrocytic anemia in alcoholic CLD patients due to folic acid and vitamin B12 deficiency.

In this study, the platelet count was normal in early stages but decreasing trend of platelet count is observed as the severity of CLD increases. The mean platelet count in group A was found to be 1.82 ± 0.443 lac/mm3; in group B 1.582 ± 0.404 lac/mm3 and in group C 0.948 ± 0.183 lac/mm3 (p = 0.00). The result is similar to the study conducted by **Qamar et al**[3], which studied that most subjects had thrombocytopenia at baseline. One hundred ninety-seven subjects had thrombocytopenia, of which 84% had it present at baseline, and 16%

developed it during the course of the study. Baseline thrombocytopenia (p = .0191) and leukopenia (p = .0383) were predictors of death or transplant, after adjusting for baseline hepatic venous pressure gradient (HVPG), and Child–Pugh scores.

In this study the MCV level was showing the increasing trend with mean MCV level in group A is 83.05 ± 7.60 fl, in group B is 89.10 ± 6.99 fl, and in group C is 93.18 ± 8.02 fl (p = 0.005). The result is more accurately observed in alcoholic CLD patients. The study done by **Shivam Khare, et al**[2] also showed the similar results where mean of MCV was compared and found that with increase in class of child pugh score MCV increases. MCV of class A alcoholic CLD was 92.5 ±12.36 & non alcoholic was 75.5 ±10.86, of class B alcoholic CLD was 85.59±16.10 & non alcoholic was 81.13±10.71 and of class C alcoholic CLD was 101.89±18.26 & non alcoholic CLD was 87.17±12.76.

In this study the MCH level did not showed any proper trend with mean MCH level in group A is 29.83 ± 1.69 pg, in group B is 30.80 ± 2.90 pg and in group C is 28.68 ± 6.63 pg (p=0.320). Even the MCHC level did not showed any significant trend with increasing severity of the disease with mean MCHC level in group A 36.34 ± 5.40 g/dl, in group B 34.81 ± 4.68 g/dl, and in group C 31.27 ± 8.97 g/dl (p=0113).

The serum vitamin B12 level significantly increases as disease severity increases. The mean vitamin B 12 level in group A 877.82 ± 314 pg/ml, in group B 1104.58 ± 145.013 pg/ml, and in group C 1338.00 ± 277.271 pg/ml (p=0.00) while the serum folic acid, in this study, showed the insignificant change with severity of the disease. The mean value of serum folic acid in 8.12 ± 3.60 ng/mL, in group B is 7.33 ± 3.99 ng/ml, and in group C is 5.21 ± 1.75 ng/ml (p=0.073),. The study conducted by **Fredrerick**[4] **et al** on CLD patients showed similar results. Fifty-five patients with liver disease of varied etiology and severity have been studied. Serum folate concentrations were subnormal and folic acid clearances rapid in 19 alcoholic cirrhotic who had a megaloblastic anemia. Eleven patients, from both the non-alcoholic and alcoholic groups, had rapid folic acid clearances, with subnormal serum folate levels in seven, in the absence of morphologic evidence of folate deficiency. Serum B12 concentrations were uniformly normal or elevated. Thirty-five patients had serum vitamin B12 levels that were within the normal range, and 19 had increased concentrations of 1000 pg/ml or greater. The degree of impairment of liver function in the 19 patients with high serum B12 levels was mild in 2, moderate in 4, and severe in 13.

In this study, we observed that as the disease severity increase, level of serum ferritin increases significantly. The mean ferritin level in group A is 184.00 ± 66.87 ng/ml, in group B is 196.25 ± 60.69 ng/ml And in group C is 267.20 ± 54.81ng/ml (p=0.001). **Büyükaşik NS et al**[5] in their study found that ferritin levels increased as Child-Pugh class progressed. S.ferritin level in patients with C.P class A was 198±254, C.P. Class B was 161±161 and C.P.Class C was 366±396. In many advanced cirrhosis cases, TS and ferritin were simultaneously elevated, which may lead to suspicion of iron overload. All of the cases with simultaneously increased TS and ferritin were Class C cirrhotic. The significant increase in serum ferritin level and decrease haemoglobin level concludes that there is chronic inflammatory condition which leads to non utilization of serum ferritin by suppressed bone marrow.

CONCLUSION

Hence this study concludes:

1. Hematological indices in CLD patients in CP Class C were having significant reduction in Hemoglobin & platelet count & increase in MCV level as compared to CP Class B & C. This could be because of advanced liver disease having continuous blood seeping from GI tract, Hypersplenism & reduced folic acid & vitamin B12 level.
2. In CP Class C, the serum vitamin B12 levels were found significantly increased as compared to CP group A & B. This could be because of disrupted liver tissue vit.B12 binding & storage by transcobalamin, which leads to leaking of vitB12 in the blood & deficiency at tissue level.[6]
3. Serum folic acid level did not show any statistically significant change.

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