Section: General Medicine

Original Research Article

HEMATOLOGICAL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE – A PROSPECTIVE STUDY FROM NAVI MUMBAI

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Abstract

Background: This study was undertaken to describe the Hematological abnormalities in decompensated chronic liver disease so that measures could be taken to correct them and reduce morbidity. **Materials and Methods:** It was a prospective observational study conducted in Department of Medicine, Dr DY Patil School of Medical and Research Centre, Nerul, Navi Mumbai in which we included CLD patients with 1 or more features of decompensation in the form of ascites, jaundice, hepatic encephalopathy or bleeding varices were included. Data were collected using a pre-designed semi-structured study proforma. **Results:** We observed that the mean hemoglobin level was 8.7 gm/dl, where 17% had hemoglobin <6 gm/dl, 38% had 6 to 8.9 gm/dl, 25% had 9 to 12.9 gm/dl and 20% had hemoglobin ≥13 gm/dl. On peripheral smear examination, 17% had normocytic anemia, 42% had microcytic anemia, 28% had macrocytic anemia and 13% had dimorphic anemia. mean TLC was 8549 per cumm, in which 7% had TLC <4000, 15% had TLC 4000 to 5999, 35% had TLC 6000 to 7999, 23% had TLC 8000 to 11000 and 20% had TLC >11000 per cumm. 10% of the patients had platelet count <1,00,000 per ml, 47% had platelet count 1,00,000 to 150,000 per ml, 35% had platelet count of 150,001 to 2,00,000 per ml and 8% had platelet count of >200,000 per ml. 7% of the patients had INR <1.1, 37% had 1.2 to 1.5, 32% had 1.6 to 2, 15% had INR 2.1 to 2.5 and 10% had INR >2.5. PT was 9 to 12 seconds in 18% and rest had prolonged PT (82%). **Conclusion:** From this study we can conclude that various haematological alterations are very common in cirrhosis patients that needs to be identified and corrected early to reduce morbidity and mortality.

INTRODUCTION

Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Multiple etiological factors lead to a similar clinico-pathological syndrome in CLDs, although the rates of progression and clinical course may be different.

With the notable exceptions of factors VIII and XIII, all of the other numbered clotting factors (II, V, VII, IX, X, XI) and the structural protein fibrinogen (factor I) are synthesized primarily in hepatocytes.[1] In addition, several anticoagulant proteins such as protein C, protein S, and antithrombin are also made there. The liver is also a site for the synthesis of a number of other proteins important to the hematopoietic system. In addition to being a minor site for the constitutive production of erythropoietin (about 10%), it is the primary site for the synthesis of thrombopoietin, a crucial growth factor in maintaining platelet mass. Control of available iron through hepatic synthesis of hepcidin in response to infection, inflammation, or replete iron stores directly affects the erythropoietic response.[2] The liver also happens to be the primary site for iron storage, containing an amount of iron in the body second only to the erythron (generally about 1 g in an adult).[3] Finally, because the liver has a central synthetic and regulatory role in lipid metabolism, the liver is responsible for the requisite membrane composition of lipids and cholesterol needed for optimal red blood cell deformability.

This study was undertaken to describe the hematological abnormalities in decompensated chronic liver disease so that measures could be taken to correct them and reduce morbidity.

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MATERIALS AND METHODS

Study design and sample size this was a prospective observational study conducted in Department of Medicine, Dr D.Y Patil School of Medical and Research Centre, Nerul, Navi Mumbai. CLD patients with 1 or more features of decompensation in the form of ascites, jaundice, hepatic encephalopathy or bleeding varices were included. Cirrhosis with Child-Pugh score of 7 or more also included as DCLD. Alcoholic and post infective, metabolic causes of liver diseases are taken for study Patients with known GIT malignancy or known primary hepatocellular carcinoma. , primary coagulation disorder. , Acute liver cell failure. Liver cell failure due to infective cause and patients with other causes of septicemia or endotoxemia other than primary liver causes. Were excluded from the study the sample size was calculated using following formulae

$N = (Z\alpha/2)\ 2 * (PQ) / E2.$ {N = Sample size

$Z\alpha/2$ = Z value at 1% error (2.58),P = Taken as 75% }(According to a study on spectrum of anaemia associated with chronic liver disease by Rosario Gonzalez-Casas et al showed anaemia of diverse aetiology occurs in upto 75% of cases of chronic liver disease.[4] As anaemia was the most important parameter studied in this study, its prevalence was taken as P)

Q = 1-P, E = Allowable error (taken as 15%) N = (2.58)2 * (0.75*0.25) / (0.15)2

N = 55.47 (minimum sample)

During the study period, we included 60 consecutive patients fulfilling the study criteria.

Data collection and Analysis

Data were collected using a pre-designed semi-structured study proforma. Blood investigations such as complete blood count, liver function test, UGI scopy and ultrasound abdomen were done for all the patients. Once the patients were confirmed as a case of decompensated chronic liver disease then the patients were said to undergo other tests such as RBC, Hb, WBC, platelets, reticulocyte count and peripheral smear. Peripheral smear was done to find the type of anaemia. A detailed history and blood investigations like complete blood count, liver function test, UGI scopy, ultrasound abdomen was done. Presenting complaints of the patients were taken in detail such as abdominal pain, abdominal distension, and decreased urine output, yellowish discolouration of urine and eyes, loss of appetite, loss of weight, early satiety and fever. Past history regarding the presence of diabetes mellitus, systemic hypertension, ischemic heart disease, tuberculosis were all got from the patient. Personal history such as alcohol intake, smoking, betel nut chewing were got from the patient. Family history of any liver disease was also noted. Patients were taken a detailed general and systemic examination. All complete blood investigations were done in pathology laboratory in our medical college and hospital.

RBC count was done in neubauers chamber using hayems fluid or auto analyser. normal value: 4.5 to 5.5 millon per cu mm.

Haemoglobin estimation: Done by sahlis method, based on the conversion of haemoglobin to acid hematin or acid analyser. normal values was considered to be 13 gm/dl.

Peripheral smear for blood picture: Low power field examination. High power field examination. Oil immersion examination.

WBC abnormality: Done by QBC method or using neubauers chamber with turks fluid. normal value 4000 to 11,000 cells per cu mm.

Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Ordinal data were expressed as absolute number and percentage. Cross tables were generated and chi square test was used for testing of associations and student t test was used for comparison of quantitative parameters. P-value < 0.05 is considered statistically significant. All analysis were done using SPSS software, version 24.0.

RESULTS

In the present study, 60 patients were included. Mean age of the patients was 42.4 ± 8.19 years, ranging from 19 to 78 years. It was observed that 45% of the patients were in the age group of 41 to 60 years. Alcoholic liver disease was the underlying etiology of CLD in 30%, hepatitis B in 25% and hepatitis C in 20%. In addition, cryptogenic liver cirrhosis (17%), autoimmune liver disease (7%) and Wilson's disease (2%) were other etiology of CLD. We observed that the mean hemoglobin level was 8.7 gm/dl, where 17% had hemoglobin <6 gm/dl, 38% had 6 to 8.9 gm/dl, 25% had 9 to 12.9 gm/dl and 20% had hemoglobin ≥13 gm/dl. Based on peripheral smear examination, 17% had normocytic anemia, 42% had microcytic anemia, 28% had macrocytic anemia and 13% had dimorphic anemia. In our study, mean TLC was 8549 per cumm, in which 7% had TLC <4000, 15% had TLC 4000 to 5999, 35% had TLC 6000 to 7999, 23% had TLC 8000 to 11000 and 20% had TLC >11000 per cumm. In the present study, 10% of the patients had platelet count <1,00,000 per ml, 47% had platelet count 1,00,000 to 150,000 per ml, 35% had platelet count of 150,001 to 2,00,000 per ml and 8% had platelet count of >200,000 per ml. We observed that 7% of the patients had INR <1.1, 37% had 1.2 to 1.5, 32% had 1.6 to 2, 15% had INR 2.1 to 2.5 and 10% had INR >2.5.PT was 9 to 12 seconds in 18% and rest had prolonged PT (82%). Similarly, APTT was 26 to 36 seconds in 13% and 87% had a prolonged APTT.

DISCUSSION

In our study, mean age of the patients was 42.4 ± 8.19 years, ranging from 19 to 78 years. It was observed that 45% of the patients were in the age group of 41

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to 60 years. In the present study, 78% of the patients were males (n=47) and rest being females (22%, n=13).

In the study by Kumar et al, 100 patients were taken and about 70 males and 30 females. Out of this, 8 males (11.4 percent) and 4 females (13.3 percent belong to younger age group, about 55 males and 20 females in the middle age group, about 7 males and 6 females in the elderly age group.

In the present study, alcoholic liver disease was the underlying etiology of CLD in 30%, hepatitis B in 25% and hepatitis C in 20%. In addition, cryptogenic liver cirrhosis (17%), autoimmune liver disease (7%) and Wilson's disease (2%) were other etiology of CLD.

In the study by Rajkumar et al, 2% of the patients had alcoholic cirrhosis were males. The etiology of chronic liver disease could not be determined in 24 % of cases but all ofthem had clinical and radiological features of cirrhosis.6 patients had Hepatitis B and 2 had Hepatitis C; all these 8 patients had cirrhosis. Autoimmune hepatitis and cirrhosis were present in 2 females.

We observed that the mean hemoglobin level was 8.7 gm/dl, where 17% had hemoglobin <6 gm/dl, 38% had 6 to 8.9 gm/dl, 25% had 9 to 12.9 gm/dl and 20% had hemoglobin ≥13 gm/dl. In addition, based on peripheral smear examination, 17% had normocytic anemia, 42% had microcytic anemia, 28% had macrocytic anemia and 13% had dimorphic anemia.

In the study by Kumar et al, it was found that 10 males (14.3 percent), 6 (20 percent) of the patients had severe anemia. In addition, 30 males (42.9 percent), 12 females (40.0 percent) had moderate anaemia and 20 males (28.6percent), 8 females (26.7 percent) had mild anaemia. About 10 males and 4 females had normal haemoglobin levels.[5] Female patients had a greater proportion of severe anaemia in other studies contrary to our study in which male patients has severe anaemia compared to females. Female patients had a greater proportion of severe anaemia in other studies contrary to our study in which male patients has severe anaemia compared to females.

In our study, mean TLC was 8549 per cumm, in which 7% had TLC <4000, 15% had TLC 4000 to 5999, 35% had TLC 6000 to 7999, 23% had TLC 8000 to 11000 and 20% had TLC >11000 per cumm. In a similar study by Kumar et al, about 24 males (34.3 percent) and 12 females (40 percent) had leucocytosis. Only 3 males (4.3 percent) and 1 females (3.3 percent) had leucopenia. Leucocytosis is more prevalent than leucopenia in decompensated chronic liver disease patients in my study of about 100 patients. about 36 patients had leucocytosis and is due to Infection (community acquired infection, nosocomial infection, spontaneous bacterial peritonitis and secondary peritonitis due to repeated peritoneal paracentesis. about 30 to 40 percent of the patients with leucocytosis had high grade fever and showed increase in polymorphs in ascitic fluid. 4 patients had leucopenia and may be due to hypersplenism.

We observed that 10% of the patients had platelet count <1,00,000 per ml, 47% had platelet count 1,00,000 to 150,000 per ml, 35% had platelet count of 150,001 to 2,00,000 per ml and 8% had platelet count of >200,000 per ml. Kumar and colleagues observed that thrombocytopenia was seen in 38 males and 18 females with (22.9 percent) of the males and (22 percent) of the females has thrombocytopenia. Severe thrombocytopenia was seen in 16 males and 6 females. 22 males and 12 females had mild to moderate thrombocytopenia. There were no patients with thrombocytosis. Remaining patients had normal platelet count.

We observed that PT was 9 to 12 seconds in 18% and rest had prolonged PT (82%). Similarly, APTT was 26 to 36 seconds in 13% and 87% had a prolonged APTT. Also, 7% of the patients had INR <1.1, 37% had 1.2 to 1.5, 32% had 1.6 to 2, 15% had INR 2.1 to 2.5 and 10% had INR >2.5. In the study by Joeimon et al, the bleeding time was prolonged only in 6 patients with thrombocytopenia indicating BT as an insensitive test. 36 patients had a prolonged INR. Among the 13 patients with upper GI bleed 9 had prolonged INR; indicating other factors play a role in GI bleed.

CONCLUSION

Based on the results of our study, we conclude that - Anemia was reported in 80% of the patients and 42% had microcytic anemia. Leukopenia was present in 7% and 20% had leucocytosis. Thrombocytopenia was present in 58% of the patients. INR was raised (>1.1) in 93% of the patients, with prolonged PT in 82%. From this study we can conclude that various haematological alterations are very common in cirrhosis patients that needs to be identified and corrected early to reduce morbidity and mortality.

Table 1: Distribution of patients according to hemoglobin levels (gm/dl)

Hemoglobin (gm/dl)	Frequency	Percent
< 6	10	17%
6 to 8.9	23	38%
9 to 12.9	15	25%
≥ 13	12	20%
Total	60	100%

Table 2: Distribution of patients according to peripheral smear findings among anemic patients (n=48)

Peripheral smear	Frequency	Percent
Normocytic anemia	10	17%
Microcytic anemia	25	42%
Macrocytic anemia	17	28%
Dimorphic anemia	8	13%
Total	60	100%

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Table 3: Distribution of patients according to total leucocyte count (per cumm)

Total leucocyte count(per cumm)	Frequency	Percent
< 4000	4	7%
4000 to 5999	9	15%
6000 to 7999	21	35%
8000 to 11000	14	23%
> 11000	12	20%
Total	60	100%

Table 4: Distribution of patients according to platelet count (per ml)

Platelet count (per ml)	Frequency	Percent
< 100,000	6	10%
100,000 to 150,000	28	47%
150,001 to 200,000	21	35%
> 200,000	5	8%
Total	60	100%

Table 5: Distribution of patients according to INR values

INR values	Frequency	Percent
< 1.1	4	7%
1.2 to 1.5	22	37%
1.6 to 2	19	32%
2.1 to 2.5	9	15%
> 2.5	6	10%
Total	60	100%

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