IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 8 Ver. XIII (Aug. 2017), PP 16-21
www.iosrjournals.org

Evaluation of Haematological Abnormalities in Decompensated Chronic Liver Disease Patients

[1*]Dr.S.Selvamani.MD, [2]Dr.Shiny Thomas
[1]*Associate Professor ,Department of General Medicine,Chengalpet Medical College &Hospital.Chengalpattu*
[2]*Junior resident in General Medicine,Department of General Medicine, Chengalpet Medical College & Hospital , Chengalpattu.*
*Corresponding Author: *Dr.S.Selvamani.MD*

Abstract: *Decompensated chronic parenchymal liver disease is one of the most common disease uncountered in day to day practice. Because of chronic disease many haemotological abnormalities are present in those 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 haemastatic abnormalities to decrease the co morbidity. The study was conducted to assess the hematological abnormalities and haemostatic derangements and the nature of hematological abnormalities to reduce the morbidity. Broadly the hematological abnormalities are viewed under abnormalities in RBCs,WBCs,Platelets, coagulation profile.*

Result of the study*: The most common anemia in cirrhosis is normochromic normocytic anemia. Microcytosis occur in patients with bleeding tendencies and macrocytosis occur mostly in alcoholics.Leucopenia occurs in a small fraction of patients and leukocytosis occurs in patients with history of repeated paracentesis and peritonitis. Eosinophilia is associated with parasitic infections. Thrombocytopenia is present in most of the cirrhosis patients and is associated with increased bleeding tendencies.Increased prothrombin time and APTT due to decreased synthesis of clotting factors.*

Conclusion*: All the cirrhosis patients must be evaluated for hematological and haemostatic abnormalities. Early treatment to correct these co morbidities can decrease the mortality.*

Date of Submission: 17 -08-2017 Date of acceptance: 04-09-2017

I. Introduction

The essential 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 maintanence of blood. Before birth it acts as a haemopoietic organ and after birth it plays an active and important role in the production of many element necessary for homeostasis and haemotopoiesis. hen 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. In addition both parenchymal hepatic disease and cholestatic jaundice may produce blood coagulation defects. Dietary deficiencies, alcoholism, bleeding and difficulties in hepatic synthesis of proteins used in blood formation or coagulation add to complexity of the problem. Spontaneous bleeding, bruising and purpura together with a history of bleeding after minimal trauma such as venepuncture, are most important indications of bleeding tendency in patients with liver disease than lab tests.

II. Aim Of The Study

1. To study the hematological abnormalities in decompensated liver disease patients.
2. To find out the incidence and type of anemia in chronic decompensated liver disease patients.
3. To detect the abnormalities in RBCs WBC in cirrhotic patients.
4. To detect platelet abnormalities
5. To assess the function of clotting factors in the patients with cirrhosis.
6. To correlate the hematological findings wih the severity of the disease.

Design Of Study

III. Materials And Methods

To assess the hematological abnormalities in chronic liver disease, the prevalence study was conducted in Chengalpattu medical college Hospital during the period from februray 2017 to July 2017. About 100 patients were selected in for this study. All the cases included in the study were admitted in the hospital ward evaluated for chronic liver disease and the hematological abnormalities. Oral consent for the clinical examination and for the lab investigations were obtained from all patients. Written consent also obtained for the special procedure like upper GI endoscopy. All the patients were interrogated regarding their symptoms, duration of illness, bleeding tendencies, abdominal distension, jaundice, oliguria. Past history regarding previous treatment of diabetes, hypertension, tuberculosis, coronary heart disease, trauma, blood transfusion, surgery needle pricks, contact with blood products. Personal history regarding alcoholism, smoking, high risk behavior also got. Family history of any liver disease was also noted. Then the entire patient was subjected to general examination and systemic examination. Patients were submitted to blood investigations.

Patients were evaluated for chronic liver disease to establish the diagnosis of cirrhosis. In patients with defects in coagulation is evidenced by increased prothrombin time or decreased platelet count, had increased bleeding tendency during bone marrow biopsy. After establishing the diagnosis patients were evaluated for hematological abnormalities. All blood investigations regarding hematological profile and PT ,APTT were done in clinical pathology laboratory in Chengalpattu medical college Hospital.

Upper Gi Endoscopy

UGI endoscopy was done at the medical gastroenterology department, after obtaining patient`s written consent. Patient was explained about the procedure, side effects. Patients were kept on over night fasting. Upper GI endoscopy was correlated with other finding to establish the diagnosis.

Inclusion Criteria

1. Adult patients presenting with signs and symptoms of chronic liver disease.
2. Patient with known GIT malignancy or known primary hepatocellular carcinoma.
3. Patients with primary coagulation disorder.
4. Liver cell failure due to infective cause like septicemia or end toxemia.

Data Analysis

This study regarding assessment of hematological profile and hemostasis was conducted among 100 inpatients in medicine department at Coimbatore Medical College Hospital. Out of 100 patients in this study, there are 80 male patients and 20 female patients. The age of patients in this study was in the range from 20 to 60.

Age in yrs	Male	Female	Total	Percentage
20 to 30	4	2	6	6%
30 to 40	26	10	36	36%
40 to 50	36	6	42	42%
50 to 60	14	2	16	16%

Most of the patients in the study were in the middle age group and only 6% were in younger age. Out of 6 patients two patients were diagnosed to have Wilson`s disease and others were of unknown etiology. Remaining 94 patients were diagnosed as chronic decompensated liver disease with pathology as cirrhosis and were of variable etiology.

Alcoholism

Among 20 female patients, none gave history of alcoholism and among the 80 male patients 62 patients were found to be alcoholics

Past History Of Jaundice

Among 100 patients only 32 patients had past history jaundice. Later serologic investigations for HBV Ag. Anti HCV antibody showed 12 patients positive for HBS Ag and two shows positive for anti HCV antibody. While coming to data analysis of investigations, among the 100 Chronic Liver Disease patient`s only 84 patients has raised bilirubin level. About 7% of the patients were with normal bilirubin level.

NO.	Symptoms	No. of cases	%
1.	Weakness &fatiguability	100	100
2.	Anorexia	100	100
3.	Nausea and/or vomiting	30	30
4.	Distension of abdomen	96	96
5.	Jaundice	60	60
6.	History of bleeding tendency	30	30

Among the 100 patients 100% had anorexia and weakness, fatigualitity. Jaundice was found in 60%. Bleeding tendency was in 30% of them.

Analysis Of Signs

No	SIGNS	No of cases	%
1.	Anaemia	36	36
2.	Jaundice	60	60
3.	Pedal edema	58	58
4.	Arterial sepsis	6	6
5.	Purpra& sepsis	8	8
6.	Gynecomastia&testicular atrophy	10	10
7.	Dilated veins over abdomen	50	50
8.	Splenomegaly	52	52
9.	Ascites	96	96
10.	Asterixis	6	6

Among the 100 patients 60% had jaundice and 30% had anemia. Splenomegaly observed in 52%. Spiders and Asterixis are obsereved in 6 patients.

Analysis Of Rbcs

Patients in the study were analysed for the presence and absence of anaemia and the characteristics of anaemia when present. 88 patients had anaemia and only twelve patients had normal hemoglobin above 12 gm%. About 32 patients had severe anaemia less than 8gm%.

Anemia In Chronic Liver Disease

Haemoglobingm%	Cases	Percentage
<6	4	4%
6 to 8	28	28%
8.1 to 10	44	44%
10.1 to 12	12	12%
12.1 to 18	12	12%
>14	Nil	

Rbc Count In Chronic Liver Disease

RBC Count	Cases	Percentage
25 to 3 million/mm3	18	18%
3 to 3.5	28	28%
3.5 to 4	32	32%
4 to 4.5	10	10%
>4.5	12	12%

Characteristics Of Anaemia

All the twelve patients with normal hemoglobin level had normochromic and normocytic blood picture. Among the 100 patients 52 patients had normochromic and normocytic anaemia, 30 patients had microcytic anaemia and 16 patients had macrocytosis. two had dimorphic anaemia, patients with microcytic anaemia showed anisocytosis and poikilocytosis. Target cells were seen in only 4 patients. Acanthocytes was not seen in any of the peripheral smears. Patients with macrocytosis had meant corpuscular volume more than 97fl.

Type Of Anaemia

Type of RBCs	Patients with anaemia	Percentage
Normocytic	52	52%
Microcytic	30	30%
Macrocytic	16	16%
Dimorphic	2	2%

Wbc Abnormalities

The analysis of WBCs was done with the total count and the differential count. The total count of WBCs range from 1050/mm^3 to 16,100/mm^3. Among the 100 patients Leukocytosis were observed in 22 patients. Eosinophilia was found in two patients. Leukocytosis were observed in patients with fever due to secondary infection of Ascites due to repeated paracentesis and eight patients had Leukocytosis due to spontaneous bacterial peritonitis. Leucopenia was present in 6% of patients. Lymphocytosis seen in 12% of patients, Eosinophilia in 2% of patients.

Wbc Count In Chronic Liver Disease

Total count in cells/mm^3	No. of patients	Percentage
<3000	6	6%
3000-6000	12	12%
6000-9000	32	32%
9000-12000	28	28%
12000	22	22%

Platelet Abnormalities

Total count in cells/mm^3	No. of patients	Percentage
<50,000	8	8%
50000-1,00,000	12	12%
1-1.5 lakhs	26	26%
1.5 – 2 lakhs	28	28%
>2 lakhs	26	26%

Thrombocytopenia was found in 46 patients among 100 cases in the study. Severe thrombocytopenia of<50,000 cell/mm^3 was found in patients with large spleen >8cms and had a history of massive hematemesis. Thrombocytopenia was associated with history of atleast an episode of hematemesis. Among the patients with severe thrombocytopenia 3 patients were found to have disseminated intravascular coagulation, later confirmed by the raised value of APTT and PT. Among the patients with normal level of platelets about 12 patients had history of atleast on episode of hematemesis. Among the 54 patients with normal platelet levels about 22 patients had mild splenomegaly and 12 patients had moderate splenomegaly. In 10 patients splenomegaly was observed in ultrasonogram only.

Serum Proteins

Patients were analysed for the estimation of serum proteins, which is the synthetic function of the liver and evaluated for albumin globulin ratio which will be altered in the chronic liver disease patients.

Total proteins gm%	No. of patients	Percentage
>6	14	14%
6 to 5	42	42%
5 to 4	42	42%
<4	2	2%

Among patients only 14% had total proteins more than 6gm% and only one patient had total protein<4gm% and others in the middle group.42% had protein in the range of 6-5gm% and 4% had 5-4% proteins range. All the patients had albumin globulin ratio reversal, which is again, favours the diagnosis of chronic liver disease.

Abnormalities In Coagulation

The liver secretes all the clotting factor except factor VIII and VWF, As we had no facility for the estimation of individual clotting factors, the patients were assessed for the coagulation profile by testing for prothrombin time and activated partial thromboplastin time. Among the 100 patients 30 patients had prolonged prothrombin time and 70 patients had normal prothrombin time. There was no correlation between the severity of jaundice and the prolongation of prothrombin time. Among the 30 patients with prolonged prothrombin time about 16 patients had history of atleast one episode of hematemesis. Bleeding time was prolonged in 20 patients who had platelet counts less than 1,00,000/mm^3 Bone marrow study was not done with the patients with low platelet count and prolonged prothrombin time due to the risk of increased bleeding. Among the 100 patients APTT prolonged in 6 patients. It was significantly raised in patients with DIC. They had history of spontaneous bleeding with internal bleeding and signs of endotoxemia. All the six had severe thrombocytopenia with platelats<50,000/mm^3

Bone marrow biopsy was done in all patients except those patients who had abnormal coagulation profile. Most of patients had normocellular bone marrow and 22% patients had hyper cellularity. There was no hypoplasia and aplastic changes.

IV. Summary

100 patients of decompensated chronic liver disease patients were studied.

1. Almost 80% of the patients had anemia in any one of the form.
2. Most common anemia in cirrhosis is normochromic normocytic anemia as inferred from the study(52%)
3. Microcytic anemia is found in 30% of studied population
4. Macrocytosis (16%) is almost common withalcoholics
5. Abnormal red cells such as microcytic, target cells, anisocytosis are found to be common in cirrhosis.
6. Leucopenia (6%) is found to be rare as per the study and Leukocytosis is more common in patients with spontaneous bacterial peritonitis and secondary peritonitis.
7. Thrombocytopenia is present in more than 30% of patients and is commonly present in the patients with splenomegaly and with the history of bleeding tendencies.
8. Prothrombin time prolonged in 46% of the patients. Asignificant rise in APTT with severe thrombocytopenia is found in DIC patients.

V. Conclusion

1. The most common anemia in cirrhosis is normochromic normocytic anemia. Microcytosis occur in patients with bleeding tendencies and macrocytosis occur mostly in alcoholics.
2. Leucopenia occurs in a small fraction of patients and leukocytosis occurs in patients with history of repeated paracentesis and peritonitis. Eosinophilia is associated with parasitic infections.
3. Thrombocytopenia is present in most of the cirrhosis patients and is associated with increased bleeding tendencies.
4. Increased prothrombin time and APTT due to decreased synthesis of clotting factors.
5. All the cirrhosis patients must be evaluated for hematological and haemostatic abnormalities. Early treatment to correct these co morbidities can decrease the mortality.

References

[1]. Marc. Ghany, Jay H. Hoofnagle; approach to liver disease 16th edition Harrison principle of Internal medicine volume 2, 1808-1813, 1855-58.
[2]. James Dooley ;Sheila Sherlock, Disease of the liver and biliary system 11th edition 4 ;47,22,364-381.
[3]. Jacquelyn J Mahar ;Sleisenger&furdtran`s Gastrointestinal and liver disease 6th edition 71,1199.
[4]. Con D A H enbury E; Schiff`s Disease of the liver,9th edition volume 2,2003,625-640.
[5]. R.W. Chapman, J.D. Collier, PC Hayes Davidson`s principle and practice of Medicine 20th edition 954-962
[6]. Vincent G Bain ; Oxford Text book of Medicine 4th edition, volume 1 667-74,508-512.
[7]. Summer skill WHJ, Molnar GD, Eye signs in Hepatic cirrhosis; New England Journal Of Medicine 1982;266 ;1244
[8]. Pirovino M, Linder R, Boss C et al, cutaneous spider Nevi in Liver cirrhosis; Hormonal investigations Klin. Wochenschr 1988; 62; 298.
[9]. Lioyd CW, Williams RH. Endocrine changes associated with cirrhosis oh liver American Journal of Medicine 1988; 4;315.
[10]. Goldman, Ausiello ; Cecil Text Book of Medicine 22nd edition 936-942
[11]. Paramo JA, Rocha E, Hemostasis in advanced liver disease semin. Thromb, Hemost 1993,19 ;184.
[12]. Hemostasis in cronic liver disease-LISMAN, T.; CALDWELL, S.H.; LEEBEEK, F.W.G.; PORTER,R.J. ;Journal of Thrombosis and Haemostasis, Volume 4,Number 9,September 2006; 2059-2060(2)
[13]. Shirley Parker Lovine; Maxwell M. Wintrobe clinical Haematology, 11th edition 1603.
[14]. Jandl, James H. The Anemia of Liver Disease; Observations on its mechanism. J Clin Invest. 1995 Mar,34(3);390-404
[15]. Eichner ,E.R., and Hillman, R.S. 1071. The evolution of anemia in alcoholic patients. American journal of medicine 50; 218-32
[16]. Tadatka ,Yamada Text book of Gastroenterology 4th edition volume2, 2415-50.
[17]. G.C. De Gruchy, Clinical Hematology in medical practice 4th edition chap 6 318.
[18]. Lindenbaum J, Lieber CS. Hematologic effects if alcohol in man in the absence of nutritional deficiency. N Engl J Med. 1989 Aug 14;281(7);333-338.
[19]. Study of hematological profile in chronic alcoholism KK Samal, BL Parija, PK Hui, SK Tripathy, K Nayak, S Mishra, SR Pattanaik, A Viswabandya-MKVH,Medical College, Berhampur.
[20]. Wu A, Chanarin I, Slavin G, Levi AJ. Folate deficiency in the alcoholic--- its relationship to clinical and hematological abnormalities, licer disease and folate stores. Br J Haematol.1975 Mar;29(3);469-478.
[21]. Hines JD. Reversible megaloblastic and sideroblastic marrow abnormalities in alcoholic patients. Br J Haematol.1969 16(1);87-101.Jan-Feb;
[22]. Klipstein F.A. et al (1965) Folate deficiency cirrhosis of liver,blood 25,443.
[23]. Zieve L. Hemolytic anemia in liver disease medicine(Baltimore) 1996;45; 497.
[24]. Bringham J (1960) Themacrocytosis of Hepatic disease thick macrocytes Blood 14,144,494.
[25]. Richard A Cooper et al(1975) An analysis of lipoproteins, bile acids and red cell membranes associated with target cells and the spur cells in patients with cirrhosis of liver.
[26]. Smith ja, Lonergan et, Sterling k. Spur cell anemia; acanthocyted in alcoholic cirrhosis. N ENGL J MED.1994 AUG 20;271;396-398.
[27]. McCormick PA. The spleen, hypersplenism, and other relationships between the liver and spleen. In; Bircher J, Benhamou J-P, McIntyre N, Rizzetto M, Rodes J, editors. Oxford textbook of clinical hepatology .Oxford: Oxford University Press 1999,787-795.

[28]. Vandeweil A, Delacroix DL, Van Hattum J. et al. characteristics of serum Immunoglobulin Ig A in alcoholic liver disease.
[29]. Younger H.M, Hadoke PWF, DillionJF et al, platelet function in cirrhosis and the role of humoral factors. Eur. J. GastrontrolHepatol 1997 9. 989.
[30]. Lindenbaum J, Hargrove RL. Thrombocytopenia in alcoholics. Ann Intern Med. 1968 Mar, 68(3);526-532
[31]. Laffi G Marra F,Gressele P et al, Evidence for a storage pool defect in platelets from cirrhosis patients with defective aggregation gastroenterology 1992.103;641.
[32]. Goulis J, Chau TN, Jordan S, Mehta AB, Watkinson A, Rolles K, Burroughs AK. Thrombocytopoietin concentrations are low in patients with cirrhosis and thrombocytopenia. Gut 1999;44; 754-758
[33]. Expression of Factor VII in the liver disease; correlations with the disease severity and impairment in the hemostasis. Blood Coagulation &Fibrinolysis. 12(3); 193-199,April 2001.
[34]. Mammen EF Coagulation defects in liver disease Med clin North Am 1994 78; 545.
[35]. Richard N Mitchell, Robins and Cotron 7th edition Homeostasis-Von Willi Brand factors 126-129.
[36]. Leebeak FWG, Kluft C, Knot EAR et al, A shift in balance between profibrinolytic and a fibrinolytic factors causes enhanced fibrinolysis in cirrhosis Gastroentrology 1991; 101; 1382.
[37]. Bakker CM, Knot KAR, Stibbe, J et al, Disseminated Intra vascular coagulation in liver disease J .Hepatol.1992;15:330
[38]. Schalm SW. The diagnosis of cirrhosis J. Hepatol 1997; 27:118
[39]. Jacobson D.S. et al, The blood and bone marrow in patients with cirrhosis of Liver (1989).
[40]. Jerrold et al (1999) Hematological observation in patients with chronic Hepatic insufficiency sternal bone marrow morphology.
[41]. Kimberc, Deller DJ and Lander H mechanism of anemia in cirrhosis 1985.
[42]. Prisi, J Hepatol (1994) Correlation of Anaemia in cirrhosis with Erythropoitein.

*Dr.S.Selvamani.MD. "Evaluation of Haematological Abnormalities in Decompensated Chronic Liver Disease Patients." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.8 (2017): 16-21