A Dissertation on

HAEMATOLOGICAL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE

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CERTIFICATE

This is to certify that this dissertation in **"HAEMATOLOGICAL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE"** is a work done by **Dr.V.M.DURAI MAVALAVAN** under my guidance during the period 2004 - 2007. This has been submitted in partial fulfillment of the award of M.D. Degree in General Medicine (Branch - I) by the Tamil Nadu Dr.M.G.R. Medical University, Chennai - 600 032.

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DECLARATION

I solemnly declare that this dissertation entitled **"HAEMATOLOGICAL ABNORMALITIES IN DECOMPENSATED CHRONIC LIVER DISEASE"** is done by me at Madras Medical College and Government General Hospital during 2004-2007 under the guidance and supervision of **Prof.Dr.D.B.SELVARAJ, M.D.** This dissertation is submitted to Tamil Nadu Dr.M.G.R. Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree General Medicine (Branch - I).

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CONTENTS

INTRODUCTION

Liver plays an important role in homeostasis. Any disease affecting the functions of liver will cause a breach in whole body homeostasis. Liver plays a major role in carbohydrate metabolism, lipid metabolism and protein metabolism. Its role in endocrine and hematological manifestations are 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 in normal and maintain the hemostasis. Liver is the storage site for iron, B_{12} and folic acid which are necessary for the normal hematopoiesis. Liver also secretes the clotting factors and the inhibitors and keep the hemostasis in equilibrium.

Hepatocellular failure, portal hypertension and jaundice may affect the blood picture. 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 a bleeding tendency in patients with liver disease than lab tests.

The hematological abnormalities in a chronic liver disease adds morbidity to the primary pathology and increases the mortality. Hence it becomes necessary to investigate the

hematological abnormalities and hemostatic abnormalities to decrease the comorbidity.

The study was conducted to assess the hematological abnormalities and hemostatic derangements and the nature of hemotological abnormalities, so that the treatment can be done towards the line to decrease the morbidity. Broadly the hematological abnormalities are viewed under :

1. Abnormalities of formed element
    a. RBCs
    b. WBCs
    c. Platelets
2. Coagulation abnormalities :
    a. Impaired synthesis of clotting factors
    b. Decreased inactivation of activated factors.

AIM OF THE STUDY

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

2. To detect the abnormalities in RBCs in a cirrhosis patient.

3. To find the type of anemia in a patient with chronic decompensated liver disease.

4. To assess the WBC abnormalities.

5. To detect the platelet abnormalities both quantitatively and qualitatively.

6. To assess the secretion and function of clotting factors in the patients with cirrhosis.

REVIEW OF LITERATURE

Liver

Liver is one of the largest organ in the body. It is the largest organ weights about 1200-1500 gm about 1/5 of total adult body weight. In infancy it is about 1/8th of birth weight. Liver is divided into 8 functional segments by various planes. They are grouped in to 4 sectors. Right anterior (V & VII), Right posterior (VI & VII), Left medial (IV) and left lateral with regard to portal, arterial supply and bile drainage.

Functions of liver

1. Formation and secretion of bile
2. Storage function

   Glycogen storage

   Lipid storage

   B_{12} and Folic acid storage

   Fat and water soluble vitamins
3. Inactivation of various substances

   Toxins

   Steroids

   Hormones
4. Secretion of plasma protein

Albumin

Fibrinogen

α1-antitrypsin

Ceruloplasmin

Haptoglobins

Transferrin

C3 component of complement

5. Synthesis of Immuno globulins,

IgG, IgM, IgA

6. Synthesis of Urea

Chronic liver disease or progression leads to irreversible chronic injury to liver parenchyma and intensive fibrosis with associated formation of regeneration nodules. The above condition is defined as cirrhosis of liver (2, 3, 4, 5, 6).

According to functional status of liver is cirrhosis it may be compensated cirrhosis or decompensated cirrhosis.

Compensated cirrhosis.

Cirrhosis discovered at routine examination or biochemical reaction with external signs and symptoms of liver failure like nausea, vomiting, indigestion, flatulence, dyspepsia, are early features in alcoholic cirrhosis. It may be suspected in patients with mild pyrexia, vascular spiders, palmar erythema, unexplained epistaxis or edema of ankles.

Firm enlargement of liver and splemomegaly may be present. Diagnosis by liver biopsy. These will be a slight increase in serum transaminase or γ-GT level. Sometimes associated portal hypertension may be present.

Decompensated cirrhosis

Patient presents with signs of liver cell failure usually of ascites, jaundice. Continuous mild fever is often due to gram negative bactremia, continuing hepatic cell necrosis or malignant transformation. Jaundice implies liver cell destruction, exceeds the capacity for regeneration and is always serious.

Chronic liver disease

Liver disease over a period of 6 months is termed as chronic liver disease.

Most common causes:

1. Chronic hepatitis C infection
2. Chronic hepatitis B infection
3. Alcohol induced
4. Fatty liver

5. Auto immuno hepatitis

6. Primary bilary cirrhosis

7. Sclerosing cholangitis

8. Hemochromatosis/Wilson's

Classification of cirrhosis based on etiology:

1. Alcoholic

2. Post necrotic or post infective HBV/HCV/HBV & HDV

3. Drugs and toxins

4. Autoimmune chronic liver disease

5. Metabolic disorders

    a. Hemochromatosis

    b. Wilson's

    c. Alpha antitrypsin deficiency

    d. Cystic fibrosis

    e. Glycogen storage disease

    f. Galactosemia

    g. Hereditary fructose intolerance

    h. Hereditary tyrosinemia

    i. Ornithine trans carbomylase deficiency.

    j. Abetalipoproteinemia

k. Porphyria

6. Biliary tract disease

a. Extra hepatic biliary obstruction

b. Intra hepatic biliary obstruction

c. Primary biliary cirrhosis

d. Primary sclerosing cholangitis

7. Venous outflow obstruction

a. Veno occlusive disease

b. Budd-chiari syndrome

c. Cardiac failure

8. Others

a. Obesity, diabetes mellitus

b. Intestinal bypass

c. Sarcoidosis

e. Indian childhood cirrhosis

Clinical features of cirrhosis

1. Weakness, muscle wasting and weigh loss

2. Low grade fever

3. Jaundice

4. Skin pigmentation

5. Ascites, Edema of legs

6. Purpura/spontaneous bruising

7. Loss of libido gonadal atrophy

8. Sparse body hair

9. White nails palmar erythema

10. Vascular spiders

Clinical manifestation in chronic liver disease is due to

(i) Portal hypertension

(ii) Hepato cellular failure

Stigmata of chronic liver disease

Face

Parotid enlargement

Loss of eye brows

Xanthelasma,

Telengectasia

Paper money skin

Shrunken facies

Hands

Pallor

Anemia

White nails

Duputyren's contracture

Palmar erythema

Clubbing

Skin

Spider nevi

Scanty body hair

Slate grey pigmentation

Scratch marks

Nutrition

Muscle wasting

Glossitis

Angular stomatitis

Anaemia

Endocrine

Gynaecomastia

Testicular atrophy

Features due to portal hypertension

Splenomegaly

Ascites

Esophageal varices

Anorectal varices

Dilated veins over abdomen

Role of liver in hematopoiesis and hemostasis

Liver plays an important role both in hematopoiesis with hemostatis Liver acts as a storage organ for vitamin B_{12} and folic acid which are necessary for the maturation of RBCS and WBCs. Liver secretes transferrin which is necessary for the transport of iron from the site of absorption to bone marrow for the synthesis of heme and RBCs production.

Liver plays a key role in B_{12} metabolism in taking part in enterohepaic circulation and also secretes transcobalamin I, necessary for the transport of B_{12} to the storage site.

Liver is one of the primary site of reticulo endothelial system, contains plenty of kupffer cells, plays an important role in immunity and secretes immunoglobulin.

Thrombopoietin, a regulator of platelet synthesis is secreted by liver.

Role of liver in hemostasis

Where the vessel is injured, three hemostatic responses are initiated.

1. The blood vessel constricts
2. Platelets adhere at the site of damage and aggregation.
3. Fibrin clot is formed and modified

The hemostatic response occurs in stepwise fashion. First the blood vessel constricts, followed it the platelets adhere aggregate and forms a temporary plug. It was reinforced with a fibrin clot, through a coagulation cascade. The fibrin clot is modified and after tissue healing, it is dissolved by fibrinolytic components.

The role of liver in hemostasis is through the synthesis of thrombopoietin, regulator of platelet production and synthesis of clotting factors. Liver is also a site of synthesis of inhibitors of coagulation cascade and also the regulator of fibrinolysis. Thus liver is a key regulator of hemostasis.

Clotting factors

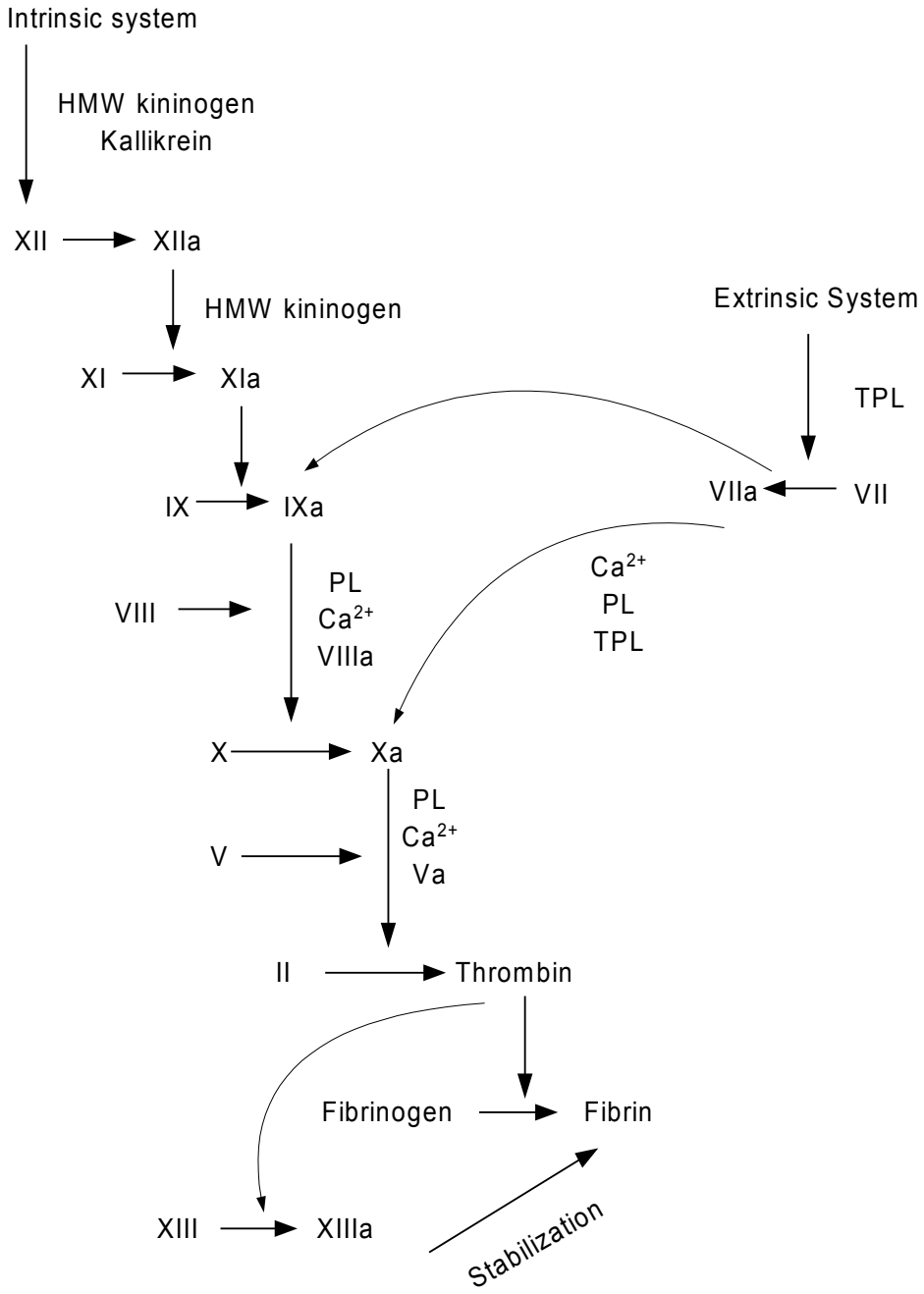
Clotting factors are the key factors in coagulation cascade. The summary of coagulation cascade as shown below.

Liver is the principal site of synthesis of all the coagulation protein with the exception of VWF and factor VIIIC. The proteins include.

Vitamin K dependant factors - II, VII, IX & X

Labile factor - V

COAGULATION CASCADE



Contact factor - XI & VII

Fibrinogen and fibrin stabilising factors

Liver is the site of vitamin K storage. The vitamin K is essential for the synthesis of factors II, VII, IX and X. The function of these blood clotting protein depends on the conversion of glutamic acid residues, post ribosomally to γ-carboxy glutamic acid by a carboxylase that requires vitamin K.

Inhibitors of coagulation cascade are also synthesized by the liver

These are Antithrombin III

Protein C & S

Heparin cofactor II

Here too protein C & S are vitamin K dependant. Liver also synthesis plasmin inhibitors such as α2-antiplasmin and tissue plasminogen activator inhibitor.

Hematological abnormalities in liver disease

Plasma volume

Plasma volume is frequently increased in patients with cirrhosis especially with ascites. Hypervolemia caused low peripheral hemoglobin or erythrocyte level.

Anemia is liver disease

Anemia occurs in 75%[34, 35] of patients with chronic liver disease. It is mostly of moderate severity and is either normochromic normocytic or moderately macrocytic in uncomplicated cirrhosis[36]. If cirrhosis is complicated with hemorrhage or hemolysis then microcytic hypochromic anaemia can occur.

Anaemia in uncomplicated cirrhosis is due to

i. Hemodilution - due to increased plasma volume.

ii. Shortened red cell survival-hypersplenism

iii. Reduced bone marrow response to anaemia due to reduced erythropoietin level, chronic inflammation and increased level of inflammatory cytokines suppress the bone marrow[4].

Patient with cirrhosis have a low oxygen -hemoglobin affinity which increased tissue oxygen availability, leads to better tolerance of anaemia[5].

Liver disease and hematinic metabolism

Iron metabolism

Low or normal serum iron concentration with a low or normal total iron binding capacity is frequently found in uncomplicated cirrhosis[6]. In alcohol induced liver disease, alcohol has toxic effect and suppresses the bone marrow but it increases the iron absorption from the GIT[7,8]. Hepatic inflammation and necrosis tend to increase serum ferritin.

The rise in MCV which accompanies CLD and alcohol ingestion masks the iron deficiency. Serum iron is bound to Beta globulin transferrin which is synthesized in liver, total iron binding capacity largely depends on the transferrin concentration. High total iron binding capacity indicates iron deficiency. TIBC is often lowered the patients with CLD due to decreased synthesis of transferrin[6]. Serum transferrin receptor level is a more reliable lab index of iron deficiency in patients with liver disease[11].

Iron deficiency also associated with hemorrhage and hemolysis. Iron deficiency causes microcytic hypochromic anaemia.

Vitamin B_{12} and Folic acid metabolism

Liver stores 5-10 mg of vitamin B_{12} representing 50-90% of body stores. Intrinsic factor is required for B_{12} absorption and there is significant enterohepatic circulation[37]. Pernicious anaemia is associated with primary biliary cirrhosis. Alcohol inhibit B_{12} absorption, elevated B_{12} binding capacity occurs in cirrhosis and hepatocellular carcinoma[12].

Liver stores of folic acid are sufficient for only 4 to 5 months[14]. Alcohol induced liver disease and poor nutrition results in disordered folate metabolism[15]. Hepatic necrosis leads to increased release of folate from liver and leads to increased urinary excretion.

Altered B12 and folate metabolism causes macrocytosis.

Hemolytic syndromes in liver disease

Red cell life span is reduced by about 50% in cirrhotic with the spleen as major site of destruction. Reticulocytosis is frequently seen in CLD. The hemolysis may be due to

Hypersplenism[16]

Lipid abnormalities

Hemolytic anaemia is also seen in Wilson's disease and in autoimmune hepatitis (Coombs positive).

Intracorpuscular defects such as instability of pyruvate kinase enzyme in alcohol CLD leads to hemolysis.

Abnormalities of red cell shape

1. Macrocytosis is seen mostly in alcoholics[18]. The increase in MCV is due to

- Increase in RBC membrane cholesterol and phospholipid content

- Reticulocytosis associated with hemorrhage and hemolysis

- Abnormalities in B12 and Folic acid metabolism

- Intrinsic abnormality in bone marrow erythropoiesis

2. Target cells bowel or saucer shaped, seen in most of CLD as their red cell membrane contains more cholesterol or more cholesterol and phospholipid

3. Echinocytes: Spiculated red cells due to changes in HDL[41] in CLD patients[20].

4. Acanthocytosis: Seen in severe liver disease. It is a bad prognostic indicator. Where it is associated with hemolytic anaemia it is called spur cell anaemia[19].

Table 1: Abnormality of RBCs

Abnormality	Primary liver disorders	Disease in other systems
Macrocytes	Many types of liver disease	Megaloblastic anaemia Hypothyroidism, cytotoxic drugs
Target cells	Many types of liver disease	Thalassaemia Other haemoglobinopathies Hyposplenism, e.g. SLE, coeliac disease
Spherocytes	Zieve's syndrome	Hereditary spherocytosis Autoimmune haemolytic anaemia Burns
Echinocytes Acanthocytes	Severe chronic liver disease Very severe disease (especially alcoholic) (Spur-cell anaemia)	Haemolytic anaemia Abetalipoproteinaemia

		Anorexia nervosa/malnutrition McLeod phenotype
Burr cells Fragmented cells (schistocytes)	Hepatorenal syndrome	Renal failure Thrombotic thrombocytopenia purpura Microangiopathic haemolytic anaemia DIC, HELLP syndrome Some haemoglobinopathies
Stomatocytes Tear-drop poikilocytes	Alcoholic cirrhosis	Alcoholism Haemolytic anaemias Primary and secondary myelofibrosis
Nucleated red cells Punctate basophilla	Acute fatty liver of pregnancy	Many causes Infections, e.g., malaria Heavy metal poisoning Haemolytic/dyserythropoietic anaemia
Rouleaux Autoagglutination Sickle cells		Myeloma/macroglobulinaemia/lymphoma Autoimmune haemolytic anaemia Sickle-cell disease

Courtesy: Oxford text book of hepatology

WBC changes in liver disease

WBC abnormalities in liver disease may be due to the underlying disease or its therapy[38]. Leucocytosis can occur in response to infection, hemorrhage, hemolysis and malignancy. Eosinophilia is frequently seen in associated with parasitic disease, hepatocellular carcinoma, hepatic.v thrombosis, drugs induced and also in primary biliary cirrhosis[26].

Leucopenia seen in CLD is due to hypersplenism or a toxic effect on bone marrow (alcohol)[24]. In neutrophil function there is a disturbance in late maturation compartment of granulocyte differentiation. Chemotaxis is inhibited. There is a low level of complement C_3[23].

Hypergamma globulinemia is a well recognised feature of cirrhosis. It is initiated by immunisation with enteric organism normally filtered by liver. IgG and IgA are markedly

increased. There is generalised immunological hyperactivity[22]. Benign monoclonal gammopathy is associated with primary biliary cirrhosis.

Platelets in liver disease

Defects of platelet number and function are well documented in patients with CLD, contributing significantly to their hemostatic abnormalities. The mechanism for thrombocytopenia are: [28,29,30]

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

There is no clear relationship between the abnormalities of platelet kinetics and the severity of liver disease as very low platelet count often accompany portal hypertension and splenomegaly in patients with relatively normal liver function[31].

There is a growing evidence of impaired platelet function in CLD and of impairment of aggregation by intrinsic platelet defects and circulating inhibitors of aggregation. Normal platelets enriched with cholesterol show increased aggregability by ADP and adrenaline[27]. Platelets in liver disease tend to be cholesterol rich but their aggregability is diminished, probably because the arachidonic acid content of platelet phospholipids is reduced.

Cross incubation studies suggested the possibility of circulating inhibitor of platelet aggregation in CLD.

HDL isolated from patients with cirrhosis inhibited ADP induced platelet aggregation, related to high apolipoprotein E content. It is also reported that basal cytosolic calcium content in platelets from cirrhosis was lower than of control. Platelets from patients with cirrhosis also exhibit a defect in VWF-binding domain. A rised level of platelet associated immunoglobulin is found in patients with CLD such as primary biliary cirrhosis, alcoholic cirrhosis, chronic active hepatitis.

Hemostasis in chronic liver disease

The abnormalities in hemostasis in CLD are due to[43,44]

i. Impaired synthesis of clotting factors.

ii. Synthesis of abnormal clotting proteins

iii. Quantitative, qualitative platelet defect

iv. Enhanced fibrinolytic activity

v. Disseminated intravascular coagulation.

Decreased clotting factor levels[46]

Factors II, VII, IX and X are vitamin K dependent clotting factors as well as the coagulation. Inhibitor Proteins C & S. Factors VII is usually first to be decreased due to its short half life. The non functional precursor forms of clotting factors are called proteins induced in vitamin K absence (PIVKA) are present due to defective carboxylation in the presence of vitamin K deficiency. Factor V is synthesized in liver in the absence of vitamin K[44]. Thus a decreased level of factor V associated with decreased levels of factor II, VII, IX and X is an indicator of hepatocellular insufficiency[46].

Hypofibrinogenemia is less frequent, until there is severe liver damage[46]. Factors XI, XII and high molecular weight kininogen are usually moderately decreased. Prekallikrein decreases early as liver disease. Factor XIII, a fibrin stabilizing factors is also decreased[48].

Decreased coagulation inhibitors

Antithrombin III is decreased in hepatocellular insufficiency. The deficiency is not severe and usually parallels that of factor V. The synthesis is only affected by general damage to liver. Protein C deficiency parallels the deficiency of other vitamin K dependent factors. The level of protein S remains significantly greater due to extrahepatic source of protein S[48].

Although levels of natural occurring inhibitors of blood clotting are decreased in hepatocellular insufficiency clinical evidence of thrombo embolism is rarely noted. This is probably due to the balance maintained between these inhibitors and the procoagulants[48].

Factors VIII is usually elevated in CLD[49], which reflects extrahepatic synthesis associated with decreased catabolism by the diseased liver. But there is some abnormality in VWF binding domain.

Fibrinogen and prothrombin

Functional abnormalities of fibrinogen molecule are known as dysfibrinogenemias[53]. Acquired dysfibrinogenemias are most often associated with CLD. Defective polymerisation results from an abnormal glycosylation of fibrinogen molecules[54]. Increased levels of sialyl transferase has been demonstrated in liver patients with dysfibrinogenemias. Impairment in fibrin formation results in prolonged thrombin time.

Abnormal type of prothrombin due to defective carboxylation is des-γ-carboxy prothrombin is increased in chronic active hepatitis, cirrhosis and hepatocellular carcinoma[55].

Fibrinolysis

Enhanced fibrinolysis is CLD is due to decreased, hepatic synthesis of inhibitors α_2-

antiplasmin and plasminogen activator inhibitor as well as decreased clearance of tissue type plasminogen activator.

Disseminated intravascular coagulation[58]

DIC is due to the consequence of non compensated formation of thrombin and leads to the formation of platelet thrombi and fibrin within the circulation[57]. Thus it is associated with activation and consumption of circulating platelets and consumption of factors V, VIII, VII, II & XIII Protein C & S, antithrombin III, plasminogen and α_2 plasmin inhibitor.

The release of tissue thromboplastin like material by necrotic liver had been the trigerring factor for DIC in severe liver failure[59]. Increased fibrinopeptide. A levels have been found in patients with cirrhosis and chronic hepatitis. Elevated level of thrombin - anti thrombin complexes have been reported in chronic active hepatitis, decompensated liver disease, end stage liver disease and fulminant liver failure.

Table - 2

Combination of haematological abnormalities with abnormal liver function tests

Abnormality	Haematological indices	Primary liver disease	Disease in other systems
Red cells anaemia	Increased MCV (macrocytic)	Many liver diseases	Alcoholism Vitamin B12/folate deficiency Haemolysis (reticulocytes up)
	Low MCV/MCHC (microcytic) Normochromic, normocytic High reticulocyte count Low reticulocyte count	With iron deficiency With dilutional anaemia With hypersplenism With marrow aplasia (viral hepatitis)	Thalassaemia Anaemia of chronic disease Haemolysis Paroxysmal noctural haemoglobinuria (± Budd-Chiari syndrome)
Normal haemoglobin Erythrocytosis	Increased MCV Low MCV	Mild liver disease With iron deficiency Hepatocellular carcinoma Viral hepatitis (rae)	Alcoholism Thalassaemia trait
White cells	Increased Neutrophils increased Lymphocytes increased Eosinophils increased	With infection, neoplasia inflammation With bacterial infection or steroid therapy Viral infections Parasitic infection Drug hepatitis Chronic active hepatitis (rarE), sarcoidosis	Myeloproliferative disorder Leukaemia, lymphoma, drugs Connective tissue disorders
	Monocytes increased Basophils/mast cells increased		Tuberculosis, Leukemia, myeloproliferative disease mastocytosis
	Decreased	With infection, marrow aplasia, or hypersplenism	Infections (typhoid, SBE, tuberculosis, septicaemia) leukaemia
	Lymphocytes decreased		Viral infections
Platelets	Increased Decreased	Liver disease And haemorhage, neoplasia inflammation With hypersplenism, viral hepatitis	Myeloproliferative disorder Leukaemia/lymphoma Connective tissue disorders Paroxysmal noctural haemoglobinuria

Courtesy: Oxford text book of hepatology

DESIGN OF STUDY

MATERIALS AND METHODS

To Assess the hematological abnormalities in chronic liver disease, the prevalence study was conducted in Government General Hospital, during the period from June 2005 to August 2006. About one hundred patients were selected in random for this study.

All of the cases in the study were admitted in the hospital ward and evaluated for chronic liver disease and for the study to assess the hematological abnormalities. Oral consent of the patients got for the clinical examination and for the lab investigations. Written consent also got for the special procedures such as liver biopsy, upper GI endoscopy and viral markers study.

All the patients were interrogated regarding the presenting complaints, duration of illness, bleeding tendencies, abdominal distension, jaundice, oliguria. Past history regarding previous treatment history, any history of diabetes, hypertension, tuberculosis, coronary heart disease. History regarding past history of any trauma, blood transfusion, surgery needle pricks, contact with blood products.

Personal history regarding alcoholism, smoking, high risk behaviour also got. Family history of any liver disease in their family member was also noted. Then the patient was subjected to general examination and systemic examination.

Patients were submitted to a number of blood investigations. Blood samples obtained from the patients were personally handed over to laboratory. The results were got in person and was noted. Blood sample were anticoagulated with EDTA.

Patients were evaluated for chronic liver disease to establish the diagnosis of cirrhosis. Liver biopsy with consent was done to confirm the diagnosis. In patients with defects in coagulation ie increased prothrombin time or decreased platelet count, there is increased bleeding tendency during liver biopsy. So in that case diagnosis is established with ultrasound and CT scan abdomen.

According to Schalm Sw. The diagnosis of cirrhosis J.Hepatol 1997; 27: 1118, ultrasound can pick up 87% of cirrhosis and should be confirmed by liver biopsy.

In the setting of contraindication to liver biopsy, suspicious of cirrhosis with ultrasound is coupled with evidence of portal gastropathy or varices in upper GI endoscopy or with portal doppler to gain more evidence of diagnosis. Above investigations were also supported with signs of liver cell failure, to establish diagnosis.

After establishing the diagnosis patients were evaluated for hematological abnormalities. All blood investigations regarding hematological profile were done in clinical pathology laboratory in Government General Hospital. Some investigations such as MCV, MCH, MCHC were done at outside lab, when the kit for testing was not available, along with all other hematological profiles, to have some control and to prevent the observers error if done separately.

Similarly prothrombin time and activated partial thromboplastin time were done at pathology laboratory, or together in laboratory outside which has same control test of PT & APTT as our pathology lab, when kits were not available in the pathology laboratory.

To assess RBC abnormality

1. RBC count:

RBC count are done in Neubauer's chamber using Hayem's fluid or auto analyser. Normal value : 4.5 to 6 million per mm^3

2. Hemoglobin estimation:

Done by Sahli's method, based on conversion of hemoglobin to acid hematin or acid analyser. Normal value : Male 14 to 18 Gm%, Female 12 to 16 Gm%.

3. Packed cell volume (PCV)

It is done in autoanalyser or using microhematocrit capillary method.

Normal value : Male 42 to 52%. Female: 37 to 47 %

4. MCV, MCHC, MCH:

- are estimated by autoanalyser

  MCV - 80 to 97 fl

  MCH - 26 to 33 pg/dl

  MCHC - 32-35 gm/dl

5. Peripheral smear for blood picture

Using stains, blood picture is examined with a lab microscope.

Low power field examination:

- Quality of film
- Number, distribution and staining of WBCs
- RBCs examination

High power field examination:

Assess RBC - Size

Shape

Hemoglobin concentration

Oil immersion examination:

Assess atypical cells and inclusion bodies

6. Reticulocyte count:

Stain - 1% brilliant cresyl blue

Normal - 0.2-2%

To assess WBC abnormality:

1. Total WBC count

Done by QBC method or using Neubauer's chamber with Turke's fluid

Normal 3,800-9,000 cells per mm^3

2. Differential count

Assessed by QBC method or direct staining and visualizing with lab microscope.

To Assess hemostasis

1. Platelet count

Manually is done by Rees-Eecker method i.e with staining with brilliant cresyl blue dye or by auto analyser.

1. Prothrombin time: Normal 10-14 sec.

2. Activated partial thromboplastin time: Normal 24-34 sec.

Liver biopsy

Liver biopsy is done with Menghini's needles under the guidance of ultrasound. Before the procedure patient written consent was got, patient was explained about the procedure and the side effects of the procedure. Patient was evaluated for any contraindications such as bleeding disorders, poor general condition, known malignancy, tense ascites. Biopsy specimen was handed over to pathologist in person and the results were collected in person.

Upper GI endoscopy

UGI endoscopy was done at medical gastroenterology department. After obtained patient's written consent, patients was explained about the procedure, side effects. Patients were kept on over night nil oral and was done upper GI endoscopy. Results were collected in person and was correlated with other finding to establish the diagnosis.

Inclusion criteria

1. All liver disease patients whose symptoms and signs persists more than 6 months

2. Alcoholic and post infective, metabolic causes of liver diseases are taken for study

Exclusion disorder

1. Patients with known GIT malignancy or known primary hepatocellular carcinoma.

2. Patients with primary coagulation disorder.

3. Acute liver cell failure

4. Liver cell failure due to infective cause and patients with other causes of septicemia or endotoxemia other than primary liver causes.

DATA ANALYSIS

This study regarding assessment of hematological profile and hemostasis was conducted among 100 inpatients in medical department at Government General hospital.

Out of 100 patients is this study, there are 80 male patients and 20 female patients. The age of patients in this study were in the range from 20 to 60.

Table 3: Age of patients

Age in yrs.	Male	Female	Total	Percentage
20 to 30	4	2	6	6%
30 to 40	25	10	35	35%
40 to 50	36	6	42	42%
50 to 60	15	2	17	17%

Most of the patients in the study were in the middle age group and only 6% were in younger age. Out of six 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 alcoholic.

Past history of jaundice

Among 100 patients only 32 patients had past history of jaundice. Later serology investigation for HBV Ag, anti HCV antibody shows 12 patients were positive for HBS Ag and only one shows positive for anti HCV antibody.

While coming to data analysis of investigations, among the 100 CLD patients only 86 patients has rised bilirubin level. About 14% of the patients were with normal bilirubin level.

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.

Table - 4: Serum proteins in CLD

Total proteins gm%	No. of patients	Percentage
>6	14	14%
6 to 5	42	42%
5 to 4	43	43%
<4	1	1%

Among 100 patients only 14% had total proteins more than 6 gm% and only one patient

had total protein <4 gm% and others in the middle group. 42% patients had protein in the range of 6-5 gm% and 43% had 5-4 gm% proteins range. All the 100 patients had albumin globulin ratio reversal, which is again towards the diagnosis of CLD.

Analysis of RBCS

Patients in the study were analysed for the presence and absence of anaemia and the characteristics of anaemia when present.

Eight eighty patients had anaemia and only twelve patients had normal hemoglobin above 12 gm%. About 32 patients had severe anaemia less than 8 gm%.

Characteristics of anaemia

All the twelve patients with normal hemoglobin level had normochromic and normocytic blood picture. Among the 88 patients 52 patients had normochromic and normocytic anaemia, 31 patients had microcytic anaemia and 16 patients had macrocytosis. Only one had dimorphic anaemia. Five patients with microcytic anaemia showed anisocytosis and poikilocytosis. Target cells were seen in only three patients. Acanthocytes was not seen in any of the peripheral smears. Patients with macrocytosis had mean corpuscular volume more than 97 fl.

Table - 5: Anemia in CLD

Haemoglobin gm%	Cases	Percentage
<6	3	3%
6 to 8	29	29%
8.1 to 10	44	44%
10.1 to 12	12	12%
12.1 to 18	12	12%
>14	Nil	

Table - 6: RBC count in CLD

Total 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%

Table - 7: Type of anaemia

Type of RBCs	Patients with anaemia	Patients with normal heamoglobin
Normocytic	52	12

Microcytic	19	
Marcrocytic	16	
Dimorphic	1	

WBC abnormalities

The analysis of WBCs were 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 leucocytosis were observed in 22 patients with lymphocytosis were observed in 12 patients. Eosinophilia was found in only two patients. Leucocytosis were observed in patients with fever due to secondary infection of ascites due to repeated paracentesis and four patients had leucocytosis due to spontaneous bacterial peritonitis. Leucopenia is present in 5% of patients. Lymphocytosis is seen in 12% of patients Eosinophilia in 2% of patients.

Table - 8: WBC Count in CLD

Total count in Cells/mm3	No. of patients	Percentage
<3000	5	5%
3000-6000	13	13%
6000-9000	32	32%
9000-12000	28	28%
>12,000	22	22%

Platelet abnormalities

Patients with platelet count less than 1.5 lakhs were carriedout to have thrombocytopenia. Among 100 patients.

Table - 9: Platelet count in CLD

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

Thrombocytopenia was found to be in 46 patients among 100 cases is the study. Severe

thrombocytopenia of <50,000 cells/mm^3 was found to be in patients with large spleen >8 cms and had a history of massive hemetemesis. Thrombocytopenia was associated with historyof atleast an episode of hematemesis. Among the patients with severe thrombocytopenia 4 patients were found to have disseminated intravascular coagulation, later confirmed by the rised value of APTT and PT and with D dimer estimation.

Among the patients with normal level of platelets about twelve patients had history of atleast one episode of hematemesis. Among the 54 patients with normal platelets level about 22 patients had mild splenomegaly and 12 patients had moderate splenomegaly. In 10 patients splenomegaly was observed in USG only.

Abnormalities in coagulation

The liver secretes all the clotting factor except factor VIII and VWF. As we have no facility for the estimation of individual clotting factors, the patients was assessed for the coagulation profile by testing for prothrombin time and activated partial thromboplastin time. Among the 100 patients 60 patients had prolonged prothrombin time and 40 patients had normal prothrombin time. There is no correlation between the severity of jaundice and the prolongation of prothrombin time.

Among the 60 patients with prolonged prothrombin time about 38 patients had history of atleast one episode of hemetemesis. Bleeding time was prolonged in 20 patients who had platelet counts less than 1,00,000/mm^3. Liver biopsy was not done with the patients with low platelet count and prolonged prothrombotin time due to the risk of increased bleeding.

Among the 100 patients APTT prolonged in almost all patients who had increased PT. It

was significantly rised in patients with DIC later confirmed by estimation of D-dimer. They had history of spontaneous bleeding with internal bleeding and signs of endotoxemia. All the four had severe thrombocytopenia with platelets <50,000/mm^3.

Bone marrow biopsy was done to all patients except those patients who had abnormal coagulation profile. Most of patients had normocellular bone marrow and eight patients had hyper cellularity. These was no hypoplastic and a plastic changes. There was no megaloblastic change.

DISCUSSION

The study involving 100 patients done at Government General Hospital has thrown light over the hematological abnormalities of chronic liver disease. The results of this study conforms with previous published reports.

RBC ABNORMALITIES

In the study we inferred that 88% of the total patients had anemia and among them 32% of cases had severe anemia.

According to studies by Kimber C, Deller DJ and Lander H. The mechanism of anemia in CLD 1965 and Sheehy W and Berman A, the anemia of cirrhosis, anemia occurs in upto 75% of patients with chronic liver disease. It is characteristically of moderate severity and is either normochromic normocytic or moderately macrocytic.

In our study 32 patients had severe anemia less than eight gm per cent. In uncomplicated cirrhosis it is rare to have such low level of hemoglobin as anemia in cirrhosis mostly due to :

i. Hemodilution

ii. Decreased erythropoietin level as per the study Siciliano Hepatol 1995 who showed decreased erythropoietin level in cirrhosis patients with anemia when compared with patients with chronic anemia due to iron deficiency.

Cirrhosis without anemia is not associated with low erythropoietin levels (Pirsi, J Hepatol 1994).

3. Chronic inflammation in cirrhosis leads to increased levels of serum inflammatory cytokines such as TNF- α, IL-1 suppress the bone marrow.

But severe anemia in cirrhosis will necessitate the investigations to rule out the following conditions :

1. Bleeding esophageal varices
2. Bleeding peptic ulcer
3. Malignancy
4. Hemolysis
5. Bleeding anorectal varices
6. Increased bleeding tendencies

In developing countries like India, people with poor socio economic state already will have nutritional anemia due to iron deficiency and B_{12} and folic acid deficiency, which is superimposed with cirrhosis leads to severe anemia. Female patients had a greater proportion of severe anemia when compared with males. It shows the poor nutritional status of women in developing countries.

SERUM PROTEINS

The plasma proteins produced by the hepatocyte are synthesized on polyribosomes bound to the rough endoplasmic reticulum, from which they are discharged into the plasma. According to Tavill AS Fall in concentration usually reflect decreased hepatic synthesis. In our study 86% of cases had decreased albumin and total protein level and all the 100 patients had albumin globulin ratio reversed. The hypoproteinemia was also contributed by poor socio economic status of the patients who got admitted at the government hospitals.

The mechanism for the low albumin level in cirrhotics is due to decreased synthetic function of liver. In cirrhosis there is a chronic inflammatory[4] process in progression which

causes elevated cytokines level such as IL-1, IL-6, TNF- α inhibits the synthesis of albumin and transferrin by the liver. In a study done by Barle H. Myberg B, Essen P, et al., the fractional synthetic rate of albumin is approximately 6% per day compared with 25% for total liver proteins. About 10 gm of albumin is synthesized by normal liver, where as with cirrhosis it synthesis only about 4 gms.

Transferrin is the iron transport protein. The plasma is more than 90% saturated with iron in patients with untreated idiopathic hemochromatosis. Reduced values may be found with cirrhosis.

CHARACTERISTICS OF ANEMIA

According to Sheila Sherlock and Oxford text book of hepatology. Most common anemia seen in cirrhotic patients is normochromic and normocytic anemia[34,35]. It is well proven in our study too. The incidence of normochromic normocytic anemia in our patients is 52%, where as in some studies there are varied results.

According to study done by Malhotra, 1951, the incidence was 90%. In studies done by Bhatia (1961) and Mishra et al., (1982), the incidence were 59% and 79% respectively.

In some studies such as Kimber C. et al., reported 43% of macocytosis, which was supported also by the study by Bingham et al.

The incidence of macrocytosis in our patients was 16%, macrocytosis in cirrhosis is mostly due to the toxic of alcohol on RBC production in the bone marrow and deficiency of B_{12} and folic acid[37]. Folic acid deficiency is also exacerbated with alcohol which was confirmed by the study done by Weir, Biochem. Pharm, 1985, and Lindenbaum.

About 19 patients in our group and microcytic hypochromic anemia. Bleeding from esophagitis, peptic ulceration or esophageal varices, compounded by the hemostatic defects of chronic liver disease, occurs in upto 70% of patients with Liver disease or per the study conducted by Kimber, Philips, et al., microcytosis in cirrohosis due to :

i. Decreased total iron concentration with alterations in iron metabolism due to decreased serum transferrin.

ii. Hemolysis due to hypersplenism, autoimmune process, lipid abnormalities or intracorpuscular defects[16].

Serum iron is bound to β globulin transferrin and total iron binding capacity largely depends on transferrin concentration. The TIBC is often lowered in cirrhosis due to reduced hepatic synthesis of transferrin.

ABNORMALITIES OF RBCS

Target cells are also thin macrocytes are found in cholestatic jaundice and hepato cellular jaundice. They have increased resistance to osmotic lysis. They are particularly prominent in cholestasis where a rise in bile acids may contribute by inhibiting lecithin cholesterol acyl transferase (LCAT) activity[65] which was proved by the study conducted by Cooper RA, Arner EC. It is seen in 2% of patients in our study.

Spur cells or acanthocytes which are associated with advanced liver disease, are bad prognostic sign[19]. They are not found in our study groups. They form because of an interaction with the abnormal HDL found in Liver disease[40].

Bone marrow of chronic hepatocellular failure is hyperplastic and macro normoblastic as per Sheila Sherlock but in our study patients with history of bleeding diasthesis patients had

hyperplastic marrow and most of the alcoholic had macro normoblastic.

ABNORMALITIES OF WBCS

According to Sheila Sherlock Leucopenia, thrombocytopenia are commonly found in cirrhotics. But according to oxford textbook of hepatology leucocyte abnormalities in liver disease may be due to the underlying disease or its therapy and range from neutrophilia to neutropenia and lymphopenia[25]. In patients with cirrhosis and systemic inflammatory response syndrome leucocyte activation is evident from measurement of leucocyte adhesion molecule expression and there is elevation of serum IL-6 evident by the study of Rosenbloom, JAMA, 1995.

In our study group all the 100 patients WBC total count are in the range of 1000 - 16,000 cell per mm^3. About 22 patients had leucocytosis which was mostly due to infections due to community required infection, nosocomial, infection, spontaneous bacterial peritonitis and secondary peritonitis due to repeated peritoneal paracentesis.

In our study group in patients with leucocytosis >12,000 / mm^3 of blood most of the patients had H/o repeated hospital admissions and had repeated paracentesis. About 50% of patients with leucocytosis had high grade fever and all patients with leucocytosis had increased cell count mostly of polymorphs in ascitic fluid analysis, which suggests the presence of peritonitis in this group of patients.

Leucopenia is present in 5% of the patients may be due to

i. Direct influences of alcohol on bone marrow.

ii. Chronic inflammatory cytokines had suppressor effect on bone marrow.

iii. Hypersplenism

iv. Infection

Eosinophilia is seen in association with parasitic diseases and also associated with Hepatic vein thrombosis, hepatocellular carcinoma[26], drug allergy and graft rejection. It is also found in primary biliary cirrhosis. Serum eosinophilic cationic protein was high in patients with primary biliary cirrhosis. Eosinophilia is present in 2% of cases in our study group mostly due to parasitic infection.

IMMUNOGLOBULINS AND LIVER DISEASE

As per the studies Feizi Gut 1968 and Jensen Arch Int Med. 1982 it has been proved that Hyperglobulinemia is a well recognised feature of cirrhosis. It has been suggested that this polyclonal hypergamaglobulinemia is initiated by immunization with enteric organisms normally filtered by the Liver[22].

Cirrhosis may be associated with a state of generalised hyperactivity, perhaps as a result of a defect of immune regulation. Berger et al., found that peripheral blood mononuclear cells from cirrhosis with hypergamaglobulinemia had a normal proportion of B cells but that IgG and IgA hypergamaglobulinemia synthesis was markedly increased. The ESR is not raised by inflammation, infection or neoplasia to the extent that one would expect is largely due to lower fibrinogen level found in cirrhotics and to the lower kininogen level.

In our study all most all patients had hypergamaglobulinemia and all the 100 cases had albumin globulin ratio reversal. The ratio reversal is also contributed by lower albumin concentration due to decreased synthesis.

PLATELETS ABNORMALITIES

Defects of platelet number and function are well documented in patients with chronic

liver disease contributing significantly to their hemostatic abnormalities[24]. Alcoholic liver disease is associated with additional abnormalities which are probably a consequence of the toxic effect of alcohol on platelet production and function is evident by the studies by Mikhaitedes BMJ, 1986, Hillbom BMJ, 1987.

There are many studies that demonstrate diverse mechanisms of thrombocytopenia. They are :

i. Shortened life span

ii. Platelet pooling in an enlarged spleen

iii. Inability of bone marrow to compensate

iv. Reduced thrombopoietin level

In our study the above findings are evident and out of 100 patients 13 patients had thrombocytopenia < 1,00,000 / mm^3 and 29 patients are i.e. the range of mild thrombocytopenia 1 - 1.5 lakhs / mm^3. All the patients with count less than one lakh had history of bleeding tendencies and among then two patients had severe thrombocytopenia < 50,000 / mm^3. Among the patients, four patients diagnosed to have DIC, which also contributed to the very low platelet count in cirrhotics.

All the patients with platelet count less than one lakh had increased bleeding time. Qualitative platelet abnormalities, assessed by template bleeding times and platelet aggregation studies may correlate with severity of chronic liver disease.[31]

ABNORMALITIES IN HEMOSTASIS

Liver plays a major role in regulating hemostasis, synthesizing most of the clotting factors and coagulation inhibitors, as well as some proteins of the fibrinolytic activated enzymes of the clotting and of the fibrinolytic systems.

As per the studies Manner EJ, 1992 and Colman RW and Rubier R.N. blood coagulation 1988, clotting factors may be decreased even before any other evidence of liver damage. In hepato cellular failure factor VII is earlier to be decreased due to its short half life then followed by factors II and X. Factor IX is usually the last to be affected[43,44].

These are vitamins K dependant proteins synthesized in Liver. If these deficiencies are unresponsive to parenteral administration of vitamin K, it can be assumed that the hepatic synthesis of clotting factors is impaired[46].

PROTHROMBIN TIME ABNORMALITIES

In our study 60 patients had elevated prothrombin value which is evident of clotting factor deficiency. They were also treated with vitamin K injection for a period of one week and the prothrombin time was repeated. Some show decrease in the prothrombin value[50,51].

Factor V synthesized in liver independent of vitamin K and decreased level of factor V along with factors, II, VII, IX and X is an indicator of hepatocellular failure[44].

APTT ABNORMALITY

APTT is prolonged in all coagulation defects including platelet activity and thromboplastin. Prolonged APTT is found in to :

1. Vitamin K deficiency
2. Liver disease
3. Presence of circulating anticoagulants
4. DIC disease

In our study four patients had found to have DIC and they have significant prolongation in APTT along with increased PT with severe thrombocytopenia. Other patients with history of bleeding tendencies had found to have moderately increased APTT.

According to oxford text book of hematology, APTT may be found to be moderately to highly prolonged according to the degree of liver failure. In case of moderate deficiencies of factor II, IX, X and V, associated with a high level of factor VIII the APTT will be normal.

DISSEMINATED INTRAVASCULAR COAGULATION

According to Sheila Sherlock, the complex changes found in coagulation proteins, inhibitors and protein fragments usually associated with DIC could have been attributed to chronic liver diseases. According to studies by Bakkar CM, knot EAR Stibbe J. et al., thrombin - antithrombin complexes, soluble fibrin and fibrinogen degradation products (D-dimer, D-monomer) suggest that low grade DIC is a component of coagulopathy in some patients with liver disease[46,58].

The mechanism stimulating this are thought to include impaired clearance of activated clotting factors and endotoxemia.

In our study four patients were found to have DIC and it was confrmed with prologation of PT and APTT along with severe thrombocytopenia and was confirmed by estimation of D-dimer. These patients were found to have septicemia, and they are culture positive showing gram negative organisms.

Thus with the above studies we inferred that many of the hematological abnormalities are to be noticed in a chronic liver disease patient, so that the comorbidity which causes increased mortality can be decreased.

From the above study we noted that the severe anemia, present in increased proportion in women than men, and is not correlated with severity of disease as evident by serum bilirubin and hypoalbuminemia. Instead it is related with history of bleeding tendency.

The character of anemia defends upon the various factors such as bleeding tendencies, dietary deficiency, alcoholism, hemolytic syndromes. But normochromic normocytic anemia is most commonly found and mostly due to the primary pathology leads to hemodilution and chronic inflammation suppressing the bone marrow.

Macrocytosis is less common in females where the incidence of alcohol is less common.

Among the Leucocyte abnormalities, leucopenia which are found in cirrhosis as per the western literature is uncommon in our study. The leucocytosis is associated with infections mostly of secondary peritonitis due to repeated paracentesis and spontaneous bacterial peritonitis.

Platelet abnormalities as assessed by Thrombocytopenia and increased bleeding time had no correlation with the severity of liver cell failure best associated in patients with large spleen and is more common in patients was bleeding tendencies, a consequence of platelet defect.

Similarly prothrombin time and APTT are prolonged is more than 50% patients which can be correlated with the liver disease and there is significant rise in APTT along with severe thrombocytopenia is seen in patients with DIC.

CONCLUSION

1. According to this study conducted with a limited cases of 100 patients, we inferred many conclusive results regarding the hematological and hemostatic abnormalities in a decompensated chronic liver disease patients.

2. In this study more than 80% of the patients had total protein less than normal and almost 100% of patients had albumin - globulin ratio reversal.

3. Almost 80% of the patients had anemia in any one of the form.

4. Most common anemia in cirrhosis is normo chromic normocytic anemia as inferred from the study.

5. Microcytic anemia is most common among women and macrocytosis is rare.

6. Macrocytosis is almost common with alcoholics.

7. Abnormal red cells such as microcytes, macrocytes, target cells, anisocytosis are found to be common in cirrhosis.

8. Leucopenia is found to be rare as per the study and Leucocytosis are more common in patients with spontaneous bacterial periotonitis and secondary peritonitis.

9. Thrombocytopenia is present is more than 30% of patients and is commonly present in the patients with splenomegaly and with the history of bleeding tendencies.

10. Prothrombin time and activated partial thromboplastin time are prolonged is more than half of the patients. A significant rise in APTT with severe thrombocytopenia is found is DIC patients.

11. Hence with this study all the cirrhosis patients must be evaluated for hematological and hemostatic abnormalities and should be monitored for any complication. Early treatment to correct these comorbidities can decrease the mortality.

SUMMARY

In our prevalence study, 100 patients admitted as inpatients at Government General Hospital are taken for our study to assess the hematological profile and the hemostatic profile. All the patients were evaluated for the diagnosis of cirrhosis. Then patients were subjected to investigations for the hematological profile and hemostatic profile. Patients were done liver biopsy, upper GI endoscopy, USG abdomen and clinical signs for the diagnosis of cirrhosis. Blood investigations were done to assess the anaemia, nature of anemia, WBCs total count and differential count, platelet count, prothrombin time and APTT.

All the investigations were collected and tabulated. According to the study, the most common anemia in cirrhotics is normochromic normocytic anaemia. Microcytosis occur in patients with bleeding tendencies and macrocytosis occur mostly in alcoholics.

Leucopenia occurs in a small fraction of patients and leucocytosis 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 are associated with increased bleeding tendencies. Most of the patients had increased prothrombin time and APTT due to decreased synthesis of clotting factors.

Thus in cirrhosis patients most of them had abnormalities in haematological parameters and hemostasis.

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ABBREVIATIONS AND ACRONYMS

CLD	:	Chronic liver disease
DCLD	:	Decompensated chronic liver disease
PT	:	Prothrombin time
APTT	:	Activated partial thromboplastin time
MCV	:	Mean corpuscular volume
MCH	:	Mean corpuscular hemoglobin
MCHC	:	Mean corpuscular hemoglobin concentration
PCV	:	Packed cell volume
TC	:	Total count
DC	:	Differential count
DIC	:	Disseminated intravascular coagulation
RBC	:	Red blood cells
WBCs	:	White blood cells
IL-1, IL-6	:	Interleukin 1, 6
TNF - α	:	Tumor necrosis factor α
TIBC	:	Total iron binding capacity
HDL	:	High density lipoprotein
ie	:	That is
CT Scan	:	Computed Tomography Scan
HBV Ag	:	Hepatitis B virus antigen
HCV	:	Hepatitis C virus

PROFORMA

Hematological profile in CLD

Name Age Sex IP No.

Occupation Address

Presenting complaints

History of present illness

Jaundice	Pedal edema
Ascites	Abdominal pain
Nausea vomiting	Fever
Hemetemesis/Melena	LOC/Fits/Confusion
Oliguria	Chest pain
	Constipation/diarrhoea
	Other symptoms

Past H/o.

Diabetes	Jaundice
Hypertension	Trauma
Ischemic heart disease	Blood transfusion
Tuberculosis	Seizures/involuntary movements
Bronchial asthma	Needle prick
Chronic kidney disease	Surgery

Malignancy Drugs

Personal H/o.

Diet

Marriage status

Smoker

Alcohol

Iv drug abuse

Sexual history

Family H/o

CLD

Wilson's

Health of members of family

Clinical examination

General examination

Built Clubbing

Nourishment Cyanosis

Conscious Pedal edema

Oriented Lymphadenopathy

Febrile

Anaemia

Jaundice

Stigmata of CLD:

Face

Telengectasia

Xanthelasma

KF ring

Parotid enlargement

Paper money skin

Loss of eye brows

Jaundice

Hands

White nails

Palmar erythema

Duputyren's contracture

Endocrine

Gynaecomastia

Testicular atrophy

Skin

Spider nevi

Scanty body hair

Slate gray pigmentation

Scratch marks

Vital signs

Pulse

Blood pressure

Temperature

Respiratory rate

Systemic examination

CVS

RS

CNS: Level of consciousness

Flapping tremors

Plantar reflex

Abdomen: Ascites Divarication of recti

Liver Umbilical hernia

Splenomegaly

Dilated veins over abdomen

Hernia and Hydrocele

Per rectal examination

Investigations

Blood	TC	**Liver function test**
	DC	S. Bilirubin
	ESR	SGOT
	Hbgm%	SGPT
	RBC Count	SAP
	PCV	γGT
	MCV	S.Albumin
	MCH	Total proteins

MCHC

Reticulocyte count

Platelet count

BT

CT

PT

APTT

Blood urea

Sugar

Creatinine

Electrolytes

Peripheral small for blood picture

Ascitic fluid:

Biochemical analysis

Cytology

Cell count

Fluid C/s

Chest X-ray

Abdomen erect x-ray

ECG in all leads

Ultrasound abdomen and pelvis

CT scan abdomen

Portal doppler

Upper GI endoscopy

Liver biopsy

Bone marrow studies

Viral markers

HBS Ag

Anti HCV antibody