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"Assessment of Hematological Abnormalities in Decompensated Chronic Liver Disease"

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I. 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, B12 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 venipuncture, 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 shall be 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 :

AIM
a. RBCs
b. WBCs
c. Platelets

2. Coagulation abnormalities:
a. Impaired synthesis of clotting factors
b. Decreased inactivation of activated factors.

OBJECTIVES
1. To assess the hematological abnormalities in a decompensated chronic liver disease patient.
a. To detect the abnormalities in RBCs
b. To find the type of anemia
c. To assess the WBC abnormalities.
d. To detect the platelet abnormalities both

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

quantitatively and qualitatively.
e. To assess the functions of clotting factors.

II. REVIEW OF LITERATURE

LIVER:

Liver is one of the largest organs in the body. It is the largest organ weights about 1200-1500 gm. 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
B12 and Folic acid storage
Fat- and water-soluble vitamins

3. Inactivation of various substances
Toxins
Steroids
Hormones

4. Secretion of plasma protein
Albumin
Fibrinogen
a1-antitrypsin
Ceruloplasmin
Haptoglobins
Transferrin
Synthesis of Immunoglobulins, IgG, IgM, IgA

5. 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.
According to functional status of liver is cirrhosis it may be compensated cirrhosis ordecompensated 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. These will be a slight increase in serum transaminase or g-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. 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

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

8. Others
a. Obesity, diabetes mellitus
b. Intestinal bypass
c. Sarcoidosis
d. 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

Nutrition
Muscle wasting
Glossitis
Angular stomatitis
Anemia

Endocrine
Gynecomastia
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[25,31] and hemostatis. Liver acts as a storage organ for vitamin B12 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 B12 metabolism in taking part in enterohepatic circulation and also secretes transcobalamin I, necessary for the transport of B12 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[56].

Role of liver in hemostasis[5,6,7,8]

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

1. The blood vessel constricts
1. Platelets adhere at the site of damage and aggregation.
2. 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[42,43,44,45].

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[34,35,36]

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

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

include.
Vitamin K dependant factors - II, VII, IX & X
Labile factor – V, Contact factor - XI & VII, Fibrinogen and fibrin stabilising factors

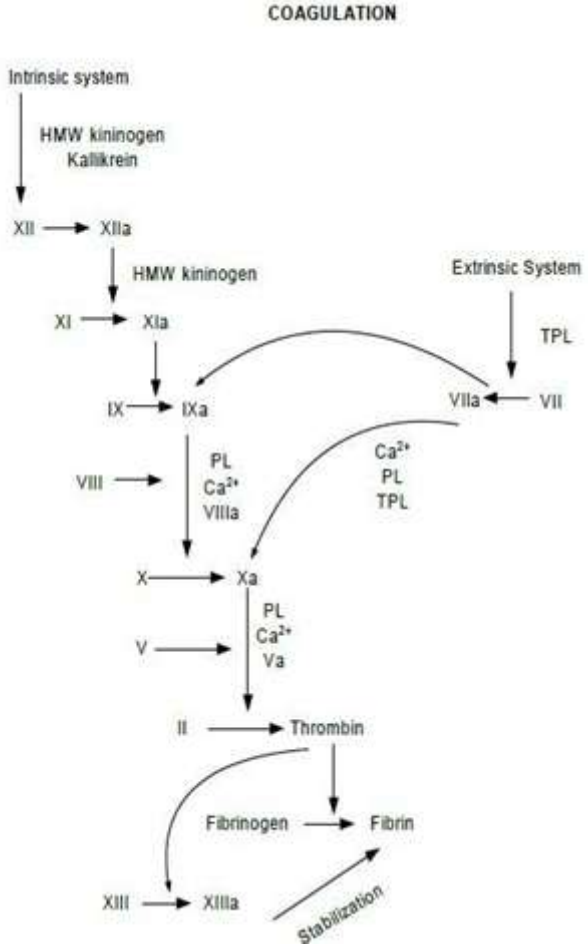


FIGURE - I: COAGULATION CASCADE

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 g-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 alpha2-antiplasmin and tissue plasminogen activator inhibitor.

Hematological abnormalities in liver disease[25,31]
Plasma volume

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

Anemia in liver disease[2]

Anemia occurs in 75%[34,35]of patients with chronic liver disease[2]. 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 anemia can occur.
Anemia in uncomplicated cirrhosis[21,23,24,26] is due to

i. Hemodilution - due to increased plasma volume.
ii. Shortened red cell survival-hypersplenism[71,75]
iii. Reduced bone marrow response to anemia due to reduced erythropoietin level, chronic inflammation and increased level of inflammatory cytokines suppress the bone marrow[27].

Patient with cirrhosis have a low oxygen - hemoglobin affinity which increases tissue oxygen availability, leads to better tolerance of anemia[2,4,5,6].

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

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. In alcohol induced liver disease, alcohol has toxic effect and suppresses the bone marrow but it increases the iron absorption from the GIT. Hepatic inflammation and necrosis tend to increase serum ferritin[6,7,8,10].

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 in 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.

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

Vitamin B12 and Folic acid metabolism[29,30]

Liver stores 5-10 mg of vitamin B12 representing 50-90% of body stores. Intrinsic factor is required for B12 absorption and there is significant enterohepatic circulation. Pernicious anemia is associated with primary biliary cirrhosis. Alcohol inhibit B12 absorption, elevated B12 binding capacity occurs in cirrhosis and hepatocellular carcinoma.

Liver stores of folic acid are sufficient for only 4 to 5 months. Alcohol induced liver disease and poor nutrition results in disordered folate metabolism. 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 anemia 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]

1. Macrocytosis is seen mostly in alcoholics[23,26]. 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 in CLD patients17.

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

TABLE - I: ABNORMALITY OF RBCS

Abnormality	**Primary liver disorders**	**Disease in other systems**
Macrocytes	Many types of liver disease	Megaloblastic anemia Hypothyroidism, cytotoxic drugs
Target cells	Many types of liver disease	Thalassaemia Other haemoglobinopathiesHyposplenism, e.g. SLE, coeliac disease

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

Spherocytes	Zieve's syndrome	Hereditary spherocytosis Autoimmune haemolyticanemia Burns
Echinocytes Acanthocytes	Severe chronic liver disease Very severe disease (especially alcoholic)(Spur-cell anemia)	HaemolyticanemiaAbetalipoproteinaemia Anorexia nervosa/malnutrition McLeod phenotype
Burr cells Fragmented cells (schistocytes)	Hepatorenal syndrome	Renal failure Thrombotic thrombocytopenia purpuraMicroangiopathichaemolyticanemia DIC, HELLP syndrome Some haemoglobinopathies
Stomatocytes Tear-drop poikilocytes	Alcoholic cirrhosis	Alcoholism Haemolyticanemias Primary and secondary myelofibrosis
Nucleated red cells Punctate basophilla	Acute fatty liver of pregnancy	Many causes Infections, e.g., malaria Heavy metalpoisoning Haemolytic/dyserythropoieticanemia
Rouleaux Autoagglutination Sickle cells		Myeloma/macroglobulinaemia/lymphoma Autoimmune haemolyticanemia Sickle-cell disease

WBC changes in liver disease[25,27,31].

WBC abnormalities in liver disease may be due to the underlying disease or itstherapy[23]. 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). In neutrophil function there is a disturbance in late maturation compartment of granulocyte differentiation. Chemotaxis is inhibited. There is a low level of complement C3[31,55,67].

Hypergammaglobulinemia 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. Benign monoclonal gammopathy is associated with primary biliary cirrhosis.

Platelets in liver disease[11,12,14,16]

Defects of platelet number and function are well documented in patients with CLD, contributing significantly to their hemostatic abnormalities. The mechanism for thrombocytopenia[51,53,54] are:

1. Shortened mean platelet life span

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

2. Platelet pooling in an enlarged spleen
3. Inability of marrow to compensate
4. Reduced thrombopoietin production[52]
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.

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[61,66,70].

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[3]

The abnormalities in hemostasis in CLD[28,29] are due to

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[31]

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[29].

Thus a decreased level of factor V associated with decreased levels of factor II, VII, IX and X is an indicator of hepatocellular insufficiency[31].

Hypofibrinogenemia is less frequent, until there is severe liver damage[31,52,59].

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[33].

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[33,35,36].

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[33].

Factors VIII is usually elevated in CLD[34], 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. Acquired dysfibrinogenemias are most often associated with CLD. Defective polymerization results from an abnormal glycosylation of fibrinogen molecules. Increased levels of sialyltransferase 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-g-carboxy prothrombin is increased in chronic active hepatitis, cirrhosis and hepatocellular carcinoma[39].

FIBRINOLYSIS

Enhanced fibrinolysis is CLD is due to decreased, hepatic synthesis of inhibitors a2-antiplasmin and plasminogen activator inhibitor as well as decreased clearance of tissue type plasminogen activator[43,44,45,46].

DISSEMINATED INTRAVASCULAR COAGULATION[47,48,49,50]

DIC is due to the consequence of non

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

compensated formation of thrombin and leads to the formation of platelet thrombi and fibrin within the circulation. 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 a2 plasmin inhibitor.

The release of tissue thromboplastin like material by necrotic liver had been the triggering factor for DIC in severe liver failure[44]. Increased fibrinopeptide. Alevels have been found in patients with cirrhosis and chronic hepatitis. Elevated level of thrombin - antithrombin complexes have been reported in chronic active hepatitis, decompensated liver disease, end stage liver disease and fulminant liver failure.

TABLE – II: COMBINATION OF HAEMATOLOGICAL ABNORMALITIES WITH ABNORMAL LIVER FUNCTION TESTS

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

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

Platelets	Increased	Liver disease And haemorhage, neoplasia inflammation	Myeloproliferative disorder Leukaemia/lymphoma Connective tissue disorders Paroxysmal noctural haemoglobinuria
	Decreased	With hypersplenism, viral hepatitis	

PLACE OF STUDY : Department of General Medicine,
Kamineni Institute of Medical Sciences, Narketpally.

STUDY DURATION : 0CTOBER-2019 to SEPTEMBER -2021
STUDY DESIGN : CROSS-SECTIONAL STUDY
SAMPLE SIZE : 50 PATIENTS
STUDY SUBJECTS : Patients Presenting with Chronic Liver Disease admitted to hospital during study period.

- Institute ethical committee clearance shall be obtained before Starting the study.
- All of the cases in the study shall be admitted in the hospital ward and evaluated for chronic liver disease and for the study to assess the hematological abnormalities.
- Oral consent from the patients will be taken for the clinical examination and for the lab investigations.
- Written consent shall be taken for special procedures such as upper GI endoscopy and viral markers study.

INCLUSION CRITERIA
1. Decompensated chronic liver disease patients whose symptoms and signs
2. Both genders are included.
3. Age group between 20-60 years persists more than 6 months

EXCLUSIONCRITERIA
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.

INVESTIGATIONS
All the patients were evaluated with complete haemogram
1. RBC count
2.Hemoglobin estimation
3. Packed cell volume (PCV)
4. MCV, MCHC, MCH
5. Peripheral smear for blood picture
6. Reticulocyte count

- Assess WBC abnormality:

1. Total WBC count 2- Differential count
- To Assess hemostasis 1- Platelet count

2. Prothrombin time
3. Activated partial thromboplastin time
- Upper GI endoscopy

III. OBSERVATION AND RESULTS

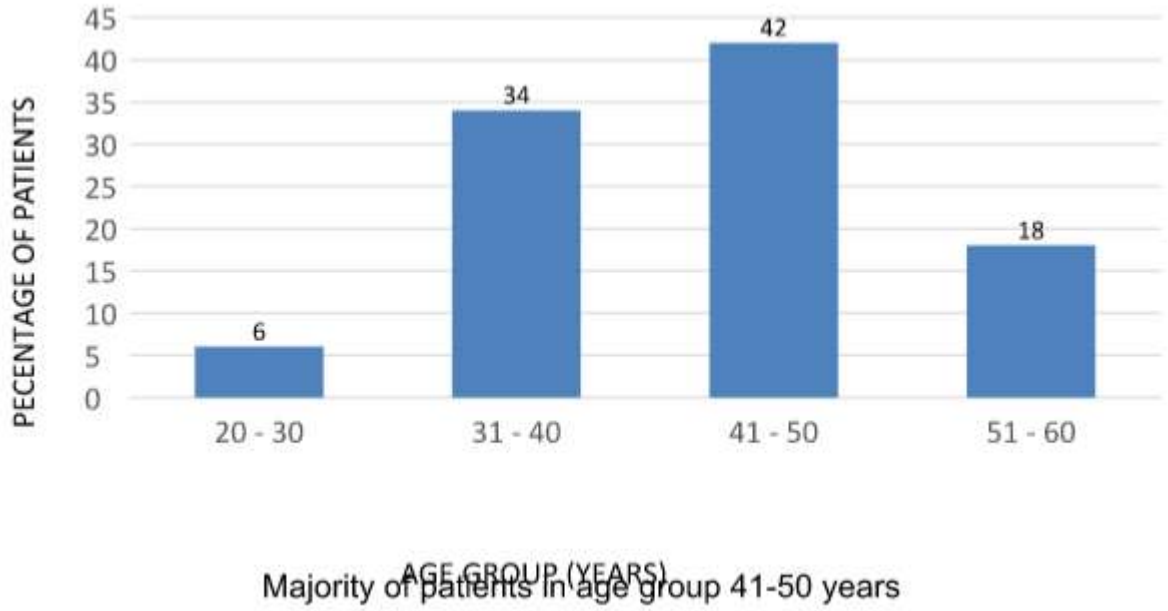
TABLE - 3:AGE DISTRIBUTIONOFPATIENTS WITH CHRONIC LIVER DISEASE(n=50)

Agein Years	Male	Female	Total	Percentage %
20–30	2	1	3	6%
31–40	16	1	17	34%
41-50	18	3	21	42%

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

51–60	7	2	9	18%

FIGURE - 2:AGE DISTRIBUTIONINYEARS vs% OF PATIENTS



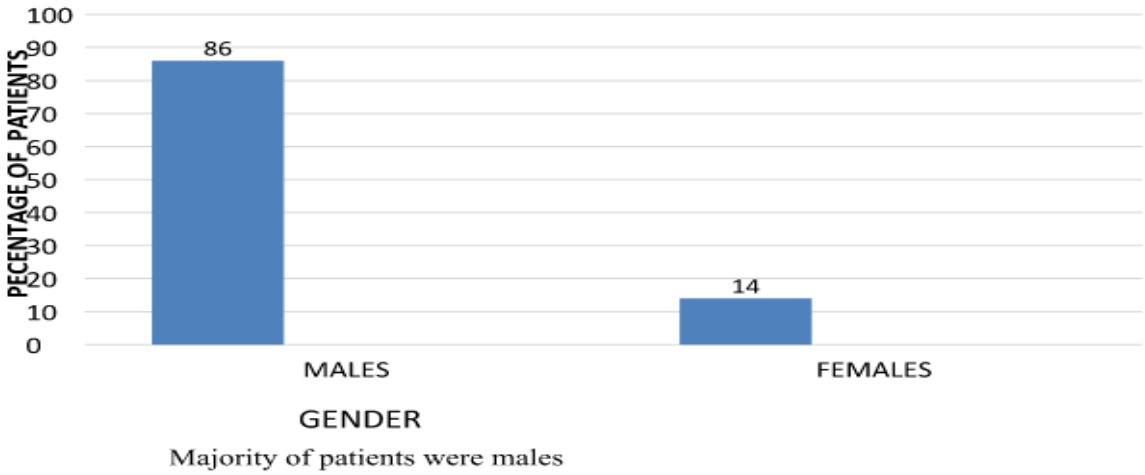
Majority of patients in age group 41-50 years

TABLE - 4: GENDERDISTRIBUTIONOFPATIENTSWITH CHRONIC LIVER DISEASE(n=50)

GENDER	**No.of Patients**	**%Patients**
Males	43	86%
Females	07	14%
Total	50	100

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

FIGURE - 3: GENDERDISTRIBUTIONOFPATIENTS vs% OF PATIENTS

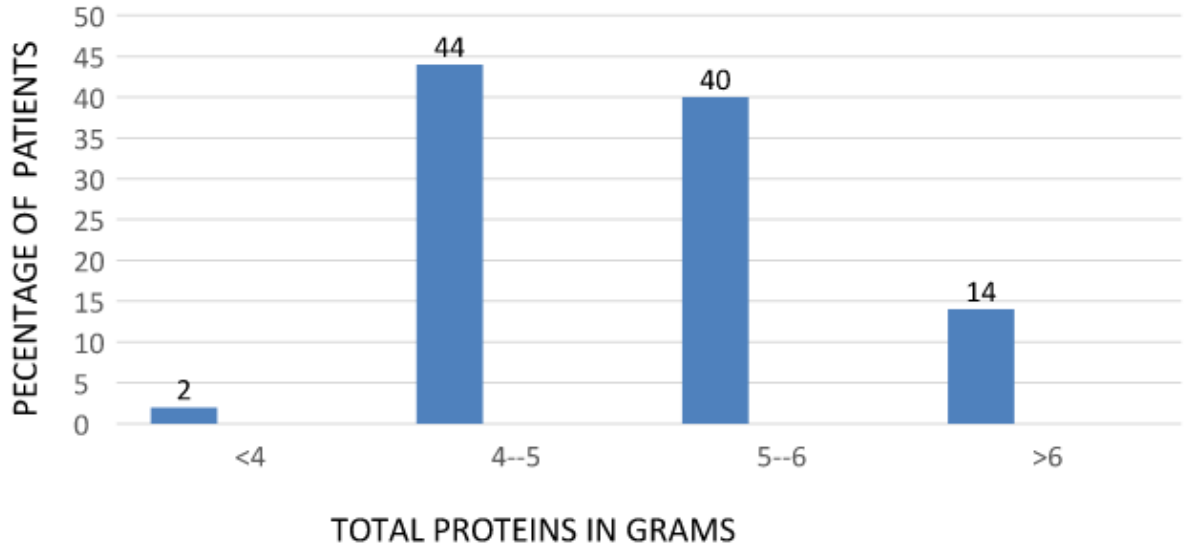


Majority of patients were males

TABLE- 5: SERUM PROTEIN LEVELSIN PATIENTSWITH CHRONIC LIVER DISEASE (n=50)

TotalProteins(gm)	No.ofPatients	%Percentage
<4	1	2
4-5	22	44
5-6	20	40
>6	7	14
Total	50	100

FIGURE - 4 : DISTRIBUTION OF SERUM PROTEIN LEVEL vs % OF PATIENTS



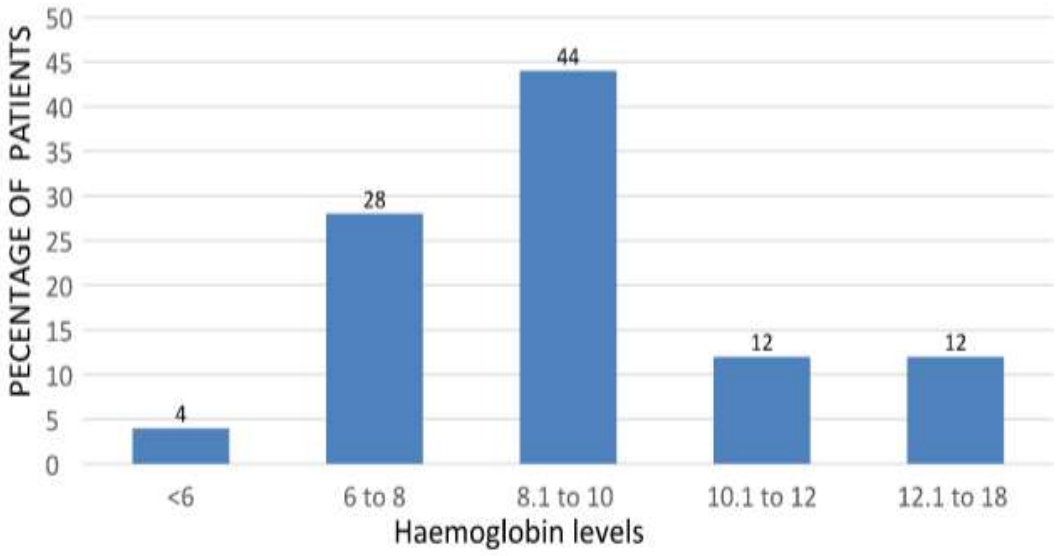
- Patients were analyzed for the estimation of serum proteins, which is the synthetic function of the liver and evaluated for albumin globulin ratio which will be altered in the chronic liver disease patients.
- Majority of chronic liver disease patients had total proteins value of 4-5 grams. All the 50 patients had albumin globulin ratio reversal, which is again towards the diagnosis of CLD.

TABLE- 6: HAEMOGLOBINLEVELS IN CHRONIC LIVER DISEASE (n=50)

Hemoglobinlevels	No.ofPatients	%Patients
<6	2	4
6-8	14	28
8.1-10	22	44
10.1-12	6	12
12.1-18	6	12
Total	50	100

No patientfound tohave haemoglobinmorethan18 gm/dl

FIGURE - 5: HAEMOGLOBIN LEVELS vs % OFPATIENTS



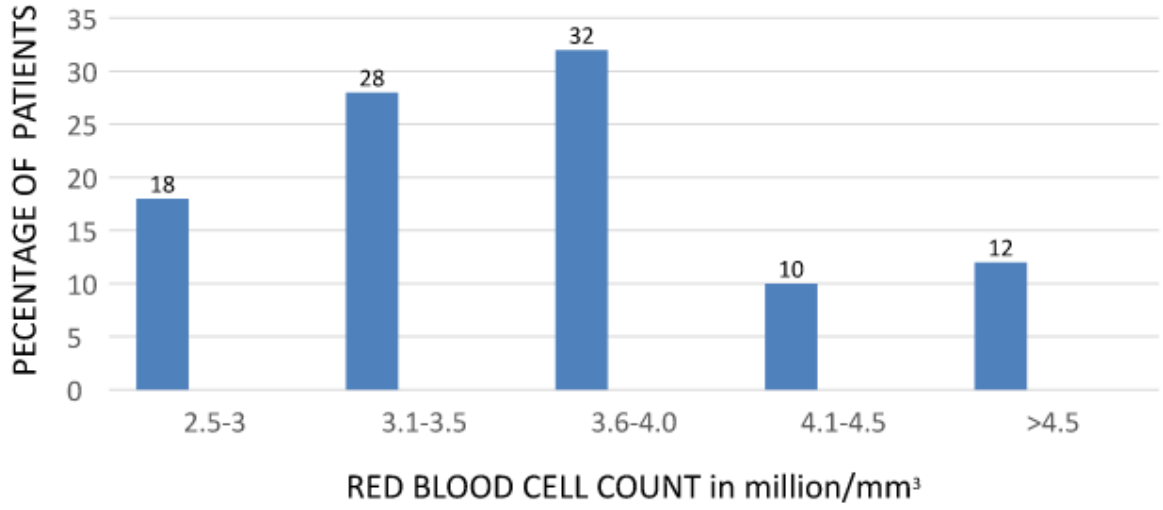
- Majority of patients had Hb levels of 8.1-10gm/dl
- 44 patients had anemia and only 6 patients had normal hemoglobin above 12 gm/dl

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

TABLE- 7: RED BLOOD CELLCOUNTIN PATIENTS WITH CHRONIC LIVER DISEASE (n=50)

TotalRBCcount Million/mm^3	No.of Patients (n=50)	%ofPatients
2.5-3	9	18
3-3.5	14	28
3.5-4	16	32
4-4.5	5	10
>4.5	6	12
Total	50	100

FIGURE - 6: RED BLOOD CELLCOUNTvs % OF PATIENTS



Majority of patients with chronic liver disease had RBC count of 3-3.5 million/mm3

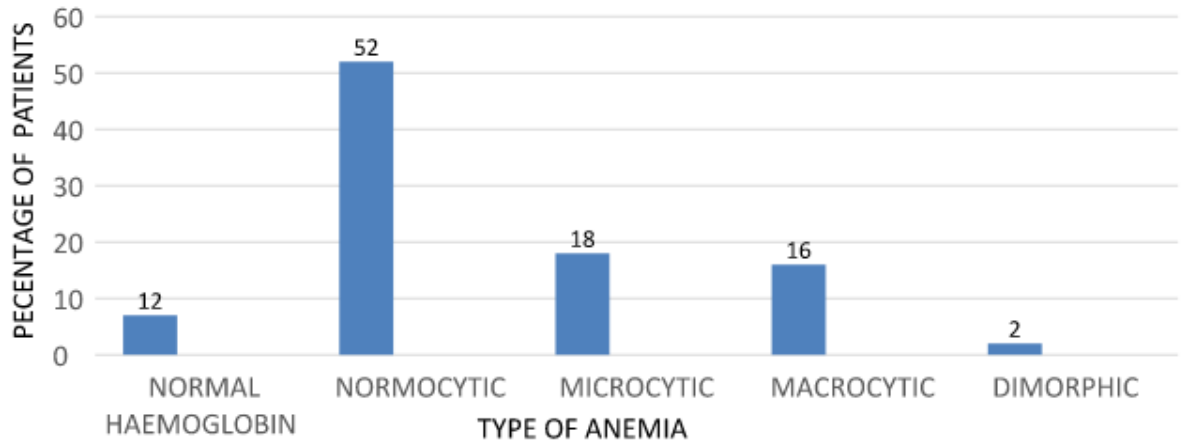
TABLE - 8:TYPES OF ANEMIAIN PATIENTS WITH CHRONIC LIVERDISEASE (n=50)

TYPESOFRBC'S	PATIENTS(N=50)	%
NORMOCYTIC	26	52
MICROCYTIC	9	18

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

MACROCYTIC	8	16
DIMORPHIC	1	2
PATIENTSWITHNORMAL HAEMOGLOBIN	6	12
TOTAL	50	100

FIGURE - 7:TYPES OFANEMIAvs % OF PATIENTS



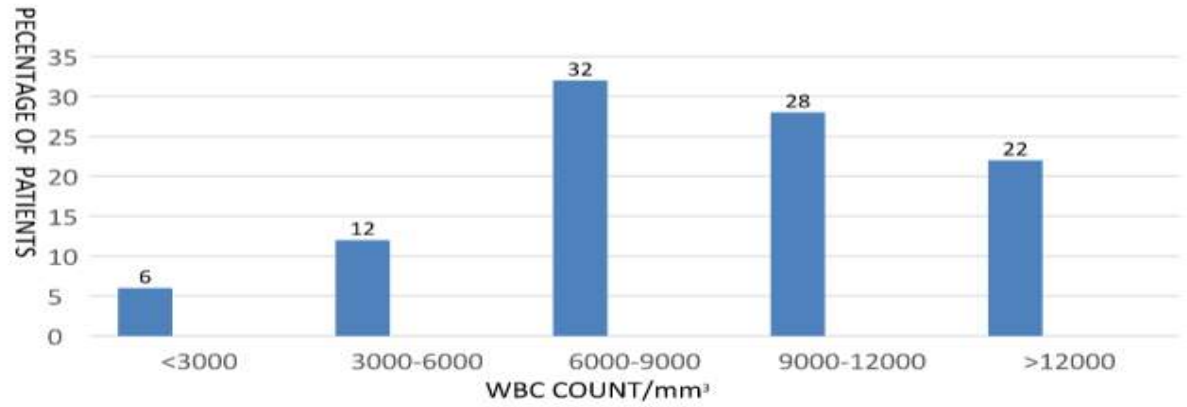
Majority of patients with chronic liver disease had normocytic anemia

TABLE- 9:WBCCOUNTIN PATIENTSWITH CHRONIC LIVER DISEASE(n=50)

TotalcountCells/mm^3	**No.ofPatients**	**Percentage%**
<3000	3	6
3000-6000	6	12
6000-9000	16	32
9000-12000	14	28
>12000	11	22
Total	50	100

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

FIGURE - 8:WBCCOUNTvs % OF PATIENTS



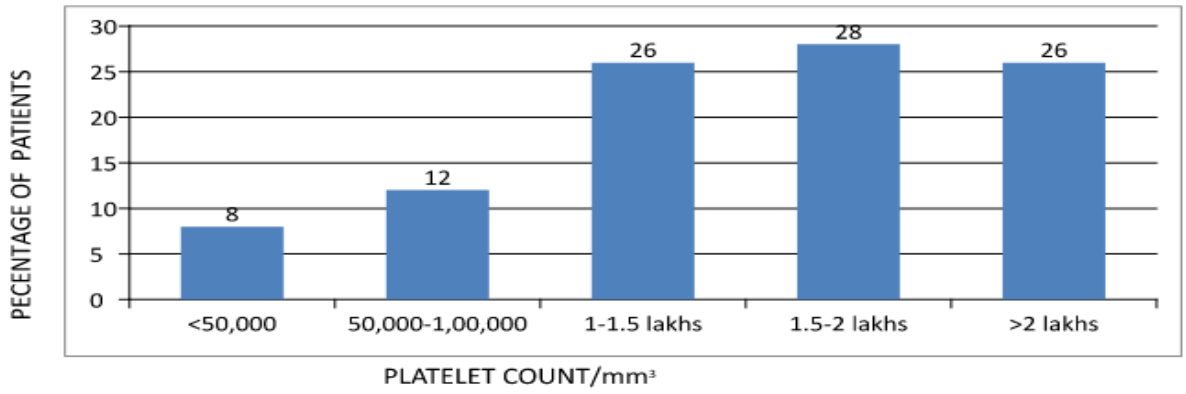
Majority of patients with chronic liver disease had WBC count of 6000-9000/mm3.

TABLE - 10: PLATELETCOUNTIN PATIENTSWITH CHRONIC LIVERDISEASE(n=50)

Plateletcountincells/mm^3	**NO.OFPatients(n=50)**	**%Percentage**
<50,000	4	8
50,000-1,00,000	6	12
1-1.5LAKH	13	26
1.5-2LAKHS	14	28
>2LAKHS	13	26
Total	50	100

WBC COUNT/mm^3

FIGURE - 9: PLATELETCOUNTvs % OFPATIENTS



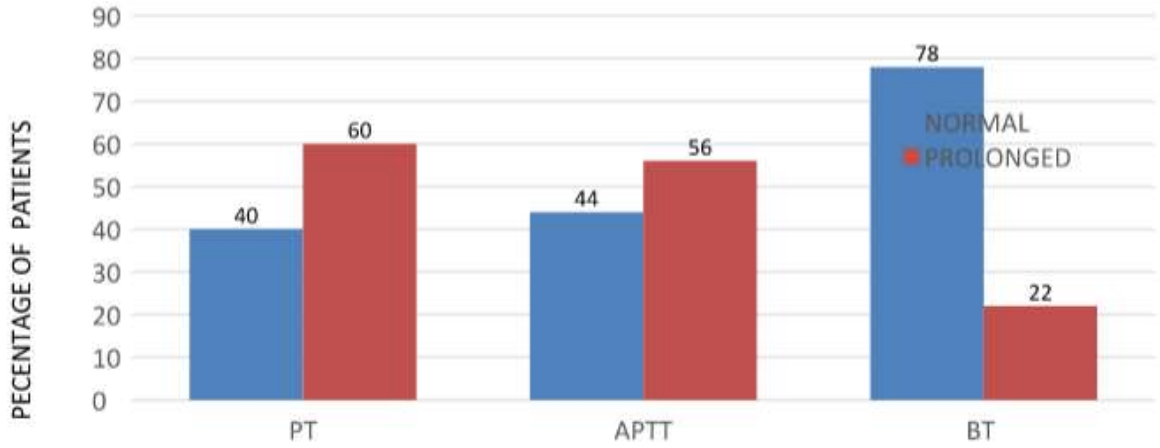
Majority of patients with chronic liver disease had platelet count in range of 1.5-2 lakhs/mm3

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

TABLE - 11: COAGULATION DISORDERSIN PATIENTS WITH CHRONIC LIVER DISEASE (n=50)

Coagulationprofile	Normal	Percentage %	Mean±SD	p-value
ProthrombinTime(seconds)	Normal	40	11.05±0.94	≤0.001
	Prolonged	60	19.23±2.70	
Activatedpartial Thromboplastin Time(seconds)	Normal	44	26.73±2.35	≤0.001
	Prolonged	56	39.96±2.16	
BleedingTime(minutes)	Normal	78	4.90±1.62	≤0.001
	Prolonged	18	10.55±0.93	

FIGURE - 10: DISTRIBUTIONOFCOAGULATION DISORDER vs % OFPATIENTS



- The liver secretes all clotting factor except factor VIII and VWF as we have no facility for the estimation of individual clotting factors the patients were assessed for coagulation profile by testing PT and APTT
- 30 patients had prolong PT and 20 patients had normal PT
- 28 patients had prolonged a PTT and majority among them had history of spontaneous bleeding.

IV. DISCUSSION

TABLE 12: DISTRIBUTION OF PATIENTS WITH CHRONIC LIVER DISEASE ACCORDING TO GENDER IN COMPARISION TO PRESENT STUDY

COMPARISIONSTUDY	DISTRIBUTION	RESULT
Anbhazganetal[2],2014,	Male	163

(n=186)	Female	23
	Ratio	7.1:1
EHalleysetal[4],2014, (n=200)	Male	164
	Female	36
	Ratio	4.6:1
Presentstudy(n=50)	Male	43
	Female	7
	Ratio	6.1 :1

- There was a clear male preponderance in the present study wand was in comparison with other studies by Anbhazgan et al and the E Halleys et al The highest risk could be attributed to the associated to the associate risk factors which prevailed in the male gender in the present study compared to females.

TABLE - 13: DISTRIBUTIONOFPATIENTSWITHCHRONICLIVER DISEASE ACCORDINGTOAGE IN COMPARISIONTO PRESENT STUDY

COMPARISIONSTUDY	DISTRIBUTION	RESULT
Anbhazganetal[2], 2014,N=186	30-50	62%
EHalleysetal[4],2014, N=200	40-60	54%
Waghmaretal[5],2011, N=196	35-55	58%
PresentstudyN=50	41-50	42%

In the present study majority of the patients are in the age group of 41-50 with 42 % which is comparable with Waghmar et al,and E Halleys et al.

TABLE - 14: COMPARISON OF ANEMIAIN PATIENTSWITH CLD

COMPARISIONSTUDY	ANEMIAIN%OFPATIENTS
Anbhazganetal[2],2014,N=186	80%

EHalleysetal[4],2014,N=200	74%
KIMBERc,DELLERDJANDLANDERH,etal[21],N=196	75%
PresentstudyN=50	88%

- 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 Anbhazgan et al,JEBMH 2015, 80% have anemia and only 10% had normal Hb above 13 gm%.
- According to studies by E Halleys et al ,WJMS 2014, 14.3% of the patients had severe anemia ,42.9% had moderate anemia and 18 % had mild anemia.
- According to studies by Kimber C, Deller DJ and Lander H. , anemia occurs in upto 75% of patients with chronic liver disease. It is characteristically of moderate severity

TABLE - 15: COMPARISON OFRED BLOODCELLCOUNTIN PATIENTS WITH CHRONIC LIVERDISEASE

COMPARISIONSTUDY	RBCCOUNT
Anbhazganet,al[2],2014,N=186	3-3.5 Million/mm3
EHalleyset,al[4],2014,N=200	3.5-4 Million/mm3
WHAGMARet,al[5],2011,N=196	3.5-4 Million/mm3
PresentstudyN=50	3.5-4 Million/mm3

Majority of patients with chronic liver disease had RBC count of 3-3.5million/mm3 in comparision to other studies.

TABLE - 16: COMPARISON OFTYPESOF ANEMIAIN PATIENTS WITH CHRONIC LIVER DISEASE

COMPARISIONSTUDY	**NormocyticNormochromictype**
Anbhazganet,al[2],2014,N=186	62.5%
EHalleyset,al[4],2014,N=200	53.85%

PresentstudyN=50	52%

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 B12 and folic acid37. Folic acid deficiency is also exacerbated with alcohol which was confirmed by the study done by Weir, Biochem. Pharm, 1985, and Lindenbaum.

ABNORMALITIESOF 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.

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 50 patients WBC total count are in the range of 1000 -16,000 cell per mm3. About 11 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 / mm3 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, 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.

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 50 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 chronicliver disease contributing significantly to their hemostatic abnormalities. Alcoholicliver disease is associated with additional abnormalities which are probably aconsequence of the toxic effect of alcohol on platelet production and function isevident by the studies by Mikhaitedes BMJ, 1986, Hillbom BMJ, 1987.

There are many studies that demonstrate diverse mechanisms ofthrombocytopenia.They are:

i. Shortened life span
ii. Platelet pooling in an enlarged spleen
iii. Inability of bone marrow to compensate
iv. Reduced thrombopoietinlevel

In our study the above findings are evident and out of 50 patients 8 patientshad thrombocytopenia < 1,00,000 / mm3 and 15 patients are i.e. the range of mild thrombocytopenia 1 - 1.5 lakhs / mm3. All the patients with count less than one lakh had history of bleeding tendencies and among then two patients had severe thrombocytopenia < 50,000 / mm3. 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.

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.

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.

PROTHROMBIN TIME ABNORMALITIES

In our study 30 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.

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.

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, Dmonomer) suggest that low grade DIC is a component of coagulopathy in some patients with liver disease.

The mechanism stimulating this are thought to include impaired clearance of activated clotting factors and endotoxemia. In present study two patients were found to have DIC and it was confirmed with prologation of PT and APTT along with severe thrombocytopenia and was confirmed by estimation of Ddimer.

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

V. SUMMARY

- In our present study, 50 patients admitted as in-patients at Kamineni institute of medical sciences are taken for our assessment to 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 upper GI endoscopy, USG abdomen and clinical signs for the diagnosis of cirrhosis
- Blood investigations were done to assess the anemia, nature of anemia, WBCs total count and differential count, platelet count, prothrombin count and APTT.
- All the investigations were collected and tabulated. According to the study, the most common anemia in cirrhotics was normochromic normocytic anemia, microcytosis occur in patients with bleeding tendencies and macrocytosis occurs 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 are associated with increased bleeding tendencies. Most of the patients had increased prothrombin time and APTT due to decreased synthesis of clotting
factors.

 Thus is cirrhosis patients most of them had abnormalities in hematological parameters and homeostasis..

VI. CONCLUSION

- According to this study conducted with 50 patients, we inferred many conclusive results regarding the hematological and hemostatic abnormalities in decompensated chronic liver disease patients.
- 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.
- Almost 80% of the patients had anemia in any one of the form.
- Most common anemia in cirrhosis is normochromic normocytic anemia as inferr ed from study.
- Microcytic anemia is most common among women and macrocytosis is rare Macrocytosis is almost common with alcoholics.
- Abnormal blood cells such as microcytes, macrocytes, target cells, anisocytosis, are found to be common in cirrhosis.
- Leucopenia is found to be rare as per study and leukocytosis is more common in patients with spontaneous bacterial peritonitis and secondary peritonitis.
- Thrombocytopenia is present in more than 30% of the patients and is commonly present in patients with splenomegaly and with history of bleeding tendencies.
- Prothrombin time and activated partial thromboplastin time are prolonged in more than half of the patients.
- Hence with this study all the cirrhosis patients must be evaluated for hematological and hemostatic abnormalities and should be monitored for any complications. Early treatment to comorbities can decrease the mortality

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ANNEXURE – I
PROFORMA

Name: Age: Sex: IPNo.
Occupation :
Address :
Presenting complaints :

History of present illness

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

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

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 HISTORY

Marriage status
Diet
Smoker
Alcohol
Iv drug abuse
Sexual history

Family H/o:

CLD
Wilson's
Health of family members

CLINICAL EXAMINATION

General examination

- Built
- Nourishment
- Conscious
- Oriented
- Febrile
- Anaemia
- Jaundice
- Stigmata of CLD:Face
- Xanthelasma
- KF ring
- Parotid enlargement
- Paper money skin
- Loss of eye brows

Clubbing
Cyanosis
Pedal edema
Lymphadenopathy

Hands Telangiectasia
Palmar erythema
Duputyren's contracture

White nails

EndocrineSkin

Gynaecomastia
Testicular atrophy

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

- Hbgm.
- RBC COUNT
- PCV
- MCV
- MCH
- MCHC
- Reticulocyte count
- Platelet count
- BT
- CT
- PT
- APTT
- Peripheral smear for blood picture

ASCITIC FLUID ANALYSIS

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
- Viral markers
- HBS Ag
- Anti HCV antibody.

ANNEXURE – II

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

CONSENT FORM
CONSENT FORM

I/ We, relative of patient have read and understood the information provided in the "Patient information sheet" and have been informed and explained the purpose and nature of the evaluation in the language I understand.

I am aware of the fact that I may not derive any benefit from the evaluation and that I reserve the right to opt out of the study at any point of time.

I willingly agree to participate in this study.

Patient's sign/thumb impression Witness's sign/thumb impression

Name: Name:

Date: Date:

Resident's sign:

Resident's Name:

Date:

ANNEXURE – III
ETHICAL COMMITTEE CLEARANCE CERTIFICATE

S. No	In Patient no.	Age	Gender	Jaundice	Ascites	HLM(V.B)	SMOKING	ALCHOHOLISM	Hb in gm/dl	RBC Ct in mill/mm3	HCT	TC/ mm3	MCV in fL	MCH in pg	MHC in %	PC /mm3	PS	TB mg/dl	DB mg/dl	AST in IU/L	ALT in IU/L	ALP in IU/L	PT in sec	APTT in sec	BT in min	HBSAG	HCV	Usg Ab
1	201927872	47	M	+	+	-	+	+	11.9	4.4	42	8700	92.3	30.4	32.4	2.56	NN	2.46	1.22	180	68	118	16	38	3	-	-	CLD
2	201928932	42	M	+	+	-	-	+	8.4	3.4	36	9800	88.4	30.6	32.9	1.46	NN	3.15	1.4	140	54	124	11	25	2	-	-	CLD
3	201940208	38	M	+	+	+	+	+	9.6	3.45	38	12100	102.6	31.9	35.6	2.42	MA	2.65	1.24	98	33	160	10	24	4	-	-	CLD
4	201946704	43	M	+	+	-	+	+	7.9	3.11	34	6500	78.4	25.4	30.2	1.62	MHA	3.65	1.6	124	46	132	18	39	3	-	-	CLD
5	201947028	39	M	+	+	-	-	+	10.5	4.71	40	12800	99.1	31.2	31.6	1.65	NN	1.22	0.62	78	19	210	13	29	5	-	-	CLD
6	202002799	48	F	+	+	+	-	+	7.6	2.74	32	8100	79.4	24.6	30.5	0.42	MHA	3.33	1.42	96	17	136	24	44	11	-	-	CLD
7	202005439	27	M	+	+	-	+	-	9.4	3.94	38	4900	96.4	26.5	32.6	1.75	NN	1.12	0.52	98	19	245	16	34	7	-	-	CLD
8	201922272	39	M	+	+	-	-	+	8.4	3.46	36	5400	84.6	31.2	32.3	1.21	NN	5.46	2.82	74	28	146	16	38	5	-	-	CLD
9	201925956	41	M	+	+	+	-	+	8.2	3.24	35	6200	92.6	28.9	34.2	1.12	NN	2.11	1.01	84	21	232	11	28	8	+	-	CLD
10	201928964	29	M	+	+	-	+	+	8.7	3.49	36	9700	104.5	32.3	35.6	2.89	MA	2.22	1.02	110	29	154	18	40	8	-	+	CLD
11	201910206	37	M	+	+	+	-	+	6.8	2.6	31	6600	96.3	33.2	32.6	2.65	NN	6.89	3.45	126	24	154	11	26	4	-	-	CLD
12	201930586	34	M	+	+	-	+	-	9.1	3.7	37	2900	102.9	31.2	35.4	1.33	MA	2.13	1.2	98	13	101	12	30	6	-	-	CLD
13	201936384	43	M	+	+	+	-	+	6.1	2.51	29	7300	74.6	21.3	29.6	0.4	MHA	5.69	2.86	124	28	168	23	43	11	-	-	CLD
14	201946150	37	F	+	+	-	-	+	9.6	3.88	39	12900	94.6	27.6	33.9	1.36	NN	2.88	1.56	74	13	269	11	24	5	-	-	CLD
15	201947851	54	M	+	+	-	+	-	8.1	3.4	35	10100	81.2	27.4	29.4	2.75	MHA	2.12	1.86	126	31	187	18	39	4	-	+	CLD
16	201947028	49	M	+	+	-	+	+	8.9	3.96	39	7200	99.8	29.6	32.5	1.89	NN	2.36	2.35	98	24	212	17	39	8	-	-	CLD
17	201948691	39	M	+	+	-	-	-	12.4	5.1	44	12100	101.2	33.5	33.6	1.39	MHA	0.98	0.42	74	13	110	20	40	4	-	-	CLD
18	201943543	58	M	+	+	+	-	+	8.3	3.43	36	7100	98.9	31.2	34.5	3.56	NN	2.33	1.12	84	21	113	12	28	3	+	-	CLD

International Journal Dental and Medical Sciences Research
Volume 5, Issue 1, Jan-Feb 2023 pp 573-601 www.ijdmsrjournal.com ISSN: 2582-6018

19	201943782	29	F	+	+	-	-	-	9.9	3.98	38	15000	102.3	33.2	33.5	1.9	MA	2.22	1.03	78	24	156	11	25	7	-	-	CLD
20	202007773	58	M	+	+	+	+	+	7.1	3.49	33	7300	81.1	25.6	29.6	0.39	MHA	2.34	1.02	124	42	114	25	45	12	-	+	CLD
21	202009420	42	M	+	+	+	-	+	8.2	3.43	35	2600	92.6	29.3	31.9	0.97	NN	3.56	1.14	98	26	169	19	40	10	-	-	CLD
22	202011707	48	M	+	+	-	-	-	13.2	5.2	46	9800	102.3	31.2	36.3	1.46	MA	6.89	3.26	154	28	187	10	26	6	-	-	CLD
23	202012433	39	M	+	+	+	+	+	8.7	3.74	36	6600	99.1	32	32.1	2.2	NN	3.65	1.82	190	34	126	22	41	4	+	-	CLD
24	202012908	54	M	+	+	-	-	+	7.9	3.44	34	17000	88.6	28.6	33.2	1.98	NN	2.36	1.12	76	17	142	20	40	3	-	-	CLD
25	202012983	38	M	+	+	-	-	+	10.4	3.98	40	5600	102.3	33.2	34.2	0.88	MHA	1.23	1.11	89	13	135	21	39	10	-	-	CLD
26	202013200	44	F	+	+	+	+	-	7.5	2.67	34	10100	93.4	31.6	32.9	1.23	NN	1.22	0.62	120	29	198	10	27	4	-	-	CLD
27	202013547	37	M	+	+	-	-	+	9.8	3.88	38	6400	90.4	27.9	31.7	2.6	NN	3.24	1.42	74	16	210	22	28	11	-	-	CLD
28	202014110	42	M	+	+	-	+	+	4.1	3.56	20	12100	72.1	24.3	29.6	1.75	MHA	6.43	3.24	68	13	265	17	39	3	+	-	CLD
29	202016106	43	M	+	+	-	-	+	8.2	3.34	35	6900	88.6	28.6	32.8	1.33	NN	2.36	1.26	72	17	213	11	27	5	-	+	CLD
30	202018450	56	F	+	+	-	-	-	12.1	4.84	43	7600	101.2	31.2	33.2	3.56	MA	1.02	0.56	98	24	145	18	39	6	-	-	CLD
31	202018664	33	M	+	+	-	+	+	9.4	3.82	37	10500	92.4	29.7	31.1	1.65	NN	1.26	0.63	124	46	241	18	38	4	-	-	CLD
32	202019344	49	M	+	+	+	-	+	6.9	2.55	31	7800	89.7	27.7	31.6	0.33	NN	1.34	0.46	136	54	153	25	46	12	-	-	CLD
33	202017890	53	M	+	+	-	+	-	8.7	3.34	36	7400	81.1	26.4	30.1	1.28	MHA	2.16	1.02	141	48	215	16	38	7	-	-	CLD
34	202019352	48	M	+	+	-	+	+	6.5	2.71	30	3900	83.4	31.1	34.6	3.36	NN	2.13	1.04	78	18	235	12	28	5	-	-	CLD
35	202020234	38	M	+	+	-	-	-	9.1	3.56	37	9700	85.6	29	32.3	1.78	NN	3.25	1.23	34	11	125	21	40	4	-	+	CLD
36	202019586	45	M	+	+	+	-	+	7.8	3.3	34	12300	79.8	26.5	29.8	1.15	MHA	2.46	1.46	88	13	124	17	39	3	-	-	CLD
37	202019723	53	M	+	+	-	-	+	9.7	3.86	38	7200	81.3	25.6	29.4	2.85	MHA	2.66	1.86	154	54	156	11	24	7	-	-	CLD
38	202023920	48	F	+	+	-	-	-	8.2	3.52	35	2400	92.8	29.9	32.5	0.96	NN	2.22	1.21	78	21	256	18	38	9	-	-	CLD
39	202026609	39	M	+	+	-	+	+	12.4	4.4	44	9400	101.6	31.2	33.2	1.54	MHA	1.22	0.64	56	13	245	10	28	6	+	-	CLD
40	202026210	44	M	+	+	+	+	+	7.2	2.64	34	10300	95.4	28.9	32.9	1.23	NN	3.25	1.89	98	16	145	17	39	5	-	-	CLD
41	2021002609	54	F	+	+	+	+	-	5.8	2.51	28	12600	96.4	27.6	31.9	0.89	NN	1.24	0.86	120	43	123	16	38	10	-	-	CLD
42	202102808	37	M	+	+	-	+	+	7.9	3.24	34	8700	87.5	28	32.1	2.96	NN	2.36	1.79	135	46	213	19	38	6	-	-	CLD
43	202106881	49	M	+	+	-	-	-	11.4	4.2	42	4900	98.6	31.4	33.9	1.39	NN	2.22	1.04	140	38	265	11	26	5	-	-	CLD
44	202108713	39	M	+	+	-	-	+	8.8	3.78	36	10900	99.9	30.6	32.6	2.34	NN	2.46	1.09	84	21	145	10	25	3	+	+	CLD
45	202116812	39	M	+	+	-	+	-	8.9	3.65	37	12700	95.4	28.4	32.4	0.79	NN	2.24	1.46	120	33	245	20	40	10	-	-	CLD
46	202110630	47	M	+	+	-	+	+	10.9	3.88	40	6200	89.6	29.4	32.5	1.69	NN	1.02	0.02	98	21	165	19	40	6	-	-	CLD
47	202112579	58	M	+	+	-	-	+	7.3	2.53	33	6900	80.1	26.5	29.5	0.74	MHA	2.36	1.22	74	26	198	21	42	10	-	-	CLD
48	202113419	42	M	+	+	-	+	+	12.4	5.2	44	5400	97.8	31.4	33.7	1.32	NN	1.02	0.06	124	39	278	10	25	3	+	+	CLD
49	202115754	39	M	+	+	-	-	+	10.1	4.3	39	11700	101.2	33.2	33.1	2.34	NN	1.98	0.86	68	35	178	13	26	4	-	-	CLD
50	202114796	49	M	+	+	-	+	+	12.1	4.7	43	12100	89.6	29.4	32.8	1.89	NN	1.02	0.56	84	41	145	11	25	6	-	-	CLD

ANNEXURE – IV
MASTER CHART
ANNEXURE – V

KEY TO MASTER CHART

Acronym	Description
M	Male
F	Female
H,M(V.B)	Hematemesis,Malena (Varecial Bleeding)
Hb	Haemoglobin
RBC CT	Red Blood Cell Count
HCT	Haematocrit
TC	Total Count
MCV	Mean Corpuscular Volume
MCH	Mean Cell Hemoglobin

MCHC	Mean Corpuscular Heamoglobin Concentration
PC	Platelet Count
PS	Peripheral Smear
TB	Total Bilirubin
DB	Direct Bilirubin
AST	Aspartate Transaminase
ALT	Alanine Transaminase
ALP	Alkaline Phosphatase
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin Time
BT	Bleeding Time
USG Abd	Ultrasound Abdomen
CLD	Chronic Liver Disease