CHAPTER I

Introduction

1.1. Introduction

The liver is a vital organ located in the upper right-hand side of the abdomen. It is weighs 2-3 pounds, and performs numerous functions for the body, converting nutrients derived from food into essential blood components, storing vitamins and minerals, regulating blood clotting, producing proteins and enzymes, maintaining hormone balances, and metabolizing and detoxifying substances that would otherwise be harmful to the body. The liver makes factors that help the human immune system fight infection, removes bacteria from the blood, and makes bile, which is essential for digestion (Baroniya, 2013).

Liver is a central regulator of the number of circulating platelets, through TPO production and clearance of aged platelets. Thrombocytopenia is a common complication of chronic liver disease, characterised by decreased TPO synthesis, reduced haematopoiesis and increased platelet destruction in the spleen. Indeed, a direct correlation between liver functionality and platelet count is often reported in patients with chronic liver disease. (Ramadori, *et al*.2019)

Liver disease is a general term that refers to any condition affecting the liver. These conditions may develop for different reasons, but they can all damage liver and impact its function. (Crystal Raypole, 2019).

A complete blood count or CBC is a blood test that measures many different parts and features of blood, including red blood cells, and their indices, white blood cells, platelet, hemoglobin and hematocrit, a measurement of how much of blood is made up of red blood these results can give the health care provider important information about overall health and risk for certain diseases. Other names for a complete blood count full blood count and blood cell count (George and Parker, 2003).

1.2. Justification

Liver responsible of producing a number of hormones and enzymes besides storing several vitamins and when it gets sick this may affect the blood cells indicators.

However the liver disease is a worldwide disease. Sudan is classified among the countries with high hepatitis B virus; hepatitis B virus was the commonest cause of chronic liver disease and hepatocellular carcinoma and was the second commonest cause of acute liver failure in the Sudan (Mudawi, 2008).

1.3. Objectives

1.3.1. General objective

To determinate complete blood count among chronic liver disease in Ibn Sina

1.3.2. Specific objective

To measure complete blood count in patients with chronic liver disease and control group

To compare between cases and control group in CBC parameters

CHAPTER II

Literature review

2.1. Introduction about liver

The liver is the largest solid organ in the body; and is also considered a gland because among its many functions, it makes and secretes bile. The liver is located in the upper right portion of the abdomen protected by the rib cage. It has two main lobes that are made up of tiny lobules. The liver cells have two different sources of blood supply. The hepatic artery supplies oxygen rich blood that is pumped from the heart, while the portal vein supplies nutrients from the intestine and the spleen (Kefelegn, 2018).

There are many different types of liver disease. But no matter what type can cause, the damage the liver is likely to progress in a similar way. Whether the liver is infected with a virus, injured by chemicals, or under attack from patient immune system, the basic danger is the same, that the liver will become so damaged that it can no longer work to keep alive. Cirrhosis, liver cancer, and liver failure are serious conditions that can threaten the life. Inflammation the early stage of any liver disease, the liver may become tender and enlarged (Lin, 2009).

2.2. Types of Liver Disease

2.2.1. **Acute liver failure**

Is a remarkably rare syndrome, the result of rapid hepatocyte injury occurring over days or a few weeks, and encompassing multiple etiologies, but all with a remarkably similar clinical picture. The clinical features of coagulopathy and encephalopathy characterize this severe and often fatal condition (Lee, 2012).

2.2.2. Chronic liver disease (CLD)

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile. CLD is a continuous process of inflammation, destruction, and regeneration of liver parenchyma, which leads to fibrosis and cirrhosis (Sharma, 2020).

CLD has diverse etiologies, which include hepatotrophic viruses, chemicals, alcohol and drug abuse, autoimmune disorders, cholestasis and metabolic diseases, and it is a major cause of morbidity and mortality in many countries. Hepatocellular carcinoma (HCC) is a

dominant complication of CLD and cirrhosis, with the third highest death rate among malignancies in the world (Kurokawa, 2017).

The following are the most common etiologies:

2.2.3. Alcoholic Liver Disease

A major cause of chronic liver disease worldwide and can lead to fibrosis and cirrhosis. The spectrum of ALD includes simple steatosis, alcoholic hepatitis, fibrosis, cirrhosis, and superimposed hepatocellular carcinoma. Early work on the pathogenesis of the disease focused on ethanol metabolism–associated oxidative stress and glutathione depletion, abnormal methionine metabolism, malnutrition, and production of endotoxins that activate Kupffer cells (Gao& Bataller, 2011).

2.2.4. Non-alcoholic Fatty Liver Disease (NAFLD)

NAFLD has an association with metabolic syndrome (obesity, hyperlipidemia, and diabetes mellitus). Some of these patients develop non-alcoholic steatohepatitis, which leads to fibrosis of the liver. All the risk factors of metabolic syndrome can aggravate the disease process (Sharma, 2020).

2.2.5. Chronic Viral Hepatitis

Chronic hepatitis B, C, and D infections are the most common causes of chronic liver disease in East Asia and Sub-Saharan Africa. There are various genotypes of hepatitis C. In Europe and North America, genotype 1a and 1b are more prevalent, while in Southeast Asia, genotype 3 is more common. A molecular epidemiological study revealed a high prevalence of HCV genotype 4, subtype 4a among Egyptian patients living in Sharkia governorate, Egypt. Chronic hepatitis C, if not treated, may lead to hepatocellular carcinoma (Sharma, 2020).

2.2.6. Genetic Causes

2.2.6.1. Alpha-1 antitrypsin deficiency

This is the most common genetic cause of CLD among children. In this inherited liver disease an important liver protein known as alpha-1 antitrypsin(A1AT) is either lacking or exists in lower than normal levels in the blood. People with alpha-1 antitrypsin deficiency are able to produce this protein; however, the disease prevents it from entering the bloodstream and it instead accumulates in the liver (Minesh, 2020).

2.2.6.2. Hereditary hemochromatosis

It is an autosomal recessive disorder of iron absorption. Here due to a mutation involving the HFE gene that regulates the iron absorption from the intestine, excessive iron is absorbed from the gastrointestinal tract. As a result, there is a pathological increase in total body iron (such as ferritin and hemosiderin). This process leads to the generation of hydroxyl free radicals, which in turn causes organ fibrosis (Sharma.2020)

2.2.6.3. Wilson disease

Autosomal recessive disorder leading to copper accumulation

2.2.7. Autoimmune Causes

(PBC), (PSC) and (AIH) represent the three major autoimmune liver diseases (AILD). PBC, PSC, and AIH are all complex disorders in that they result from the effects of multiple genes in combination with as yet unidentified environmental factors. Recent genome-wide association studies have identified numerous risk loci for PBC and PSC that host genes involved in innate or acquired immune responses (Carbone, 2014).

2.2.9. Liver Cirrhosis

Cirrhosis is a morphologic term that has been used for almost 200 years to denote the end stage of a variety of chronic liver diseases. The term implies a condition with adverse prognosis due to the well-known complications of portal hypertension, hepatocellular carcinoma, and liver failure (Hytiroglou, 2012).

Cirrhosis is the scarring of the liver - hard scar tissue replaces soft healthy tissue. As cirrhosis becomes worse, the liver will have less healthy tissue. If cirrhosis is not treated, the liver will fail and will not be able to work well or at all (Lin, 2009).

2.2.10. Liver Fibrosis

Its terminal or late stage, cirrhosis, refer to the deposition of abnormal amounts of extracellular matrix proteins, principally by activated HSCs. Patients initially exhibit active pericellular fibrosis, which may progress to cirrhosis, the late stage of hepatic scarring. However, some degree of hepatitis likely is always present in cirrhotic patients, whereas hepatic fat usually is not prominent in these individuals (Osna, *et* al 2017)

2.2.11. End-Stage Liver Disease

Liver failure is a life-threatening condition that demands urgent medical care. When liver failure occurs as a result of cirrhosis, it usually means that the liver has been failing

gradually for some time, possibly for years. Chronic liver failure or End-stage Liver Disease (ESLD) can also be caused by malnutrition. More rarely, liver failure can occur suddenly, in as little as 48 hours. This is called acute liver failure and is usually a reaction to poisoning or a medication overdose (Heidelbauch and Bruderly, 2006).

2.2.12. Liver Cancer

Cancer that starts in the liver is called primary liver cancer. Cirrhosis and hepatitis B are leading risk factors for primary liver cancer. But cancer can develop in the liver at any stage in the progression of liver disease (Heidelbauch and Bruderly, 2006)

2.3. Thrombopoietin and platelets

Thrombopoietin (TPO) is the most important factor in the regulation of megakaryocyte proliferation and differentiation into platelets through activation of its cognate receptor c-Mpl, also known as TPO-R. Several agonists of the c-Mpl receptor, such as eltrombopag and romiplostim (Kurokawa, 2017).

2.4. TPO and CLD

TPO mRNA expression is reduced in cirrhotic livers. Liver fibrosis (grade 3⁄4) and liver function correlate with low TPO serum levels. Thus, TPO serum levels in CLD are inappropriately low for the actual degree of thrombocytopenia. The gradual decline in liver function in the patients with cirrhosis and thrombocytopenia was accompanied by a gradual decline in TPO production. This resulted in a low platelet production rate by the bone marrow, ruling out a high turnover state caused by increased platelet destruction in cirrhosis. Thus, TPO serum levels reflect TPO degradation by platelets and megakaryocytes and platelet turnover and not just TPO production in the liver (Peck, 2017)

2.5. Laboratory liver tests

2.5.1. Liver Enzyme Tests

(ALT) is an enzyme mainly found in liver, the ALT test measures the level of ALT in blood. Consistently high levels of ALT in blood can be a sign of liver damage. (AST) is an enzyme found in large amounts in liver and other parts of body, the AST test measures the level of AST in blood. High levels of AST can be a sign of liver damage. (ALP) is an enzyme found in large amounts in liver, bile ducts, and other parts of body. The ALP test measures the level of ALP in blood. High levels of ALP can be a sign of liver or bile duct damage. (GGT) is an enzyme found in large amounts in liver, bile ducts, and pancreas. The

GGT test measures the level of GGT in blood. High levels of GGT can be a sign of liver or bile duct damage (Tran&Lim, 2021).

2.5.2. Liver Protein Tests

Total Protein measures the amount of protein in blood. The two main proteins found in the blood are globulins and albumin. Globulin is a protein made in liver and helps the immune system fight infections. Low globulin levels can be a sign of liver damage or other conditions. Albumin is another protein made in liver. An albumin test measures how well liver is making the proteins that body needs. Low albumin levels can be a sign of liver damage. Prothrombin is a protein made in liver and helps with clotting blood. PT test measures how much time it takes for blood to clot. A high PT can be a sign of liver damage. Bilirubin is a yellow fluid made in body when red blood cells break down. A bilirubin test measures the level of bilirubin in blood. If liver is damaged, bilirubin can leak out of liver into blood and can cause jaundice (yellowing of skin and eyes). It also can come out in the urine making it look very dark (Tran&Lim, 2021).

2.6. Blood Cells

2.6.1. White blood cell (leukocyte)

White blood cells (WBCs, Leukocytes) are nucleated cells produced from bone marrow; they have a role in body immunity. They form the first line of defense of the body against invading microorganisms. White blood cells are classified either as polymorphonuclear leucocytes (or granulocytes) or as mononuclear cells. Granulocytes are further divided into three subtypes, Neutrophils, eosinophils, and basophils. Mononuclear cells indicate both lymphocytes and monocytes (Daboul. 2019)

2.6.1.1. Leukopenia

Leukopenia is a condition where a person has fewer white blood cells in their bloodstream than they should. Leukopenia is diagnosed with a blood test called a complete blood count or CBC, healthy white blood cell count is between 3,500 and 11,000 white blood cells per microliter. A person with leukopenia may have fewer than 3,500 white blood cells per microliter. There are five kinds of leukopenia, each one corresponding to the type of white blood cell that is affected. (Lana Burgess, 2017)

2.6.1.2. Leukocytosis

An increase in white blood cells is known as leukocytosis. It typically occurs in response to the (Infection, immunosuppressant, medications, including corticosteroids, a bone marrow or immune disorder, certain cancers, such as acute or chronic lymphocytic leukemia, inflammation, injury, emotional stress, labor, pregnancy ,smoking, allergic reactions and excessive exercise).Certain respiratory illnesses, such as a whooping cough or tuberculosis, may cause the levels of white blood cells to increase (Lori Smith. 2018).

2.6.2. Red Blood Cells (Erythrocytes)

Erythrocytes constitute approximately forty percent of the total amount of the blood and ninety nine percent of shaped elements in the blood. They are biconcave disk shaped cells with an average diameter of 6.2-8.2 micrometer; one millimeter cube of blood contains 5.1 million to 5.8 million erythrocytes in men and 4.3 million to 5.2 million red blood cells in women. These numbers may vary according to age, gender, and height of place (Anil Tombak, 2019).

The primary function of red blood cells is to transport oxygen to body cells and deliver carbon dioxide to the lungs. A red blood cell has what is known as a biconcave shape. Both sides of the cell's surface curve inward like the interior of a sphere. This shape aids in a red blood cells ability to maneuver through tiny blood vessels to deliver oxygen to organs and tissues (Regina Bailey, 2019).

Hemoglobin gives red blood cell their characteristic reddish color. Blood is a brighter in the arteries as more oxygen is attached and darker and in the venous blood because of less oxygenation. It’s interesting to note that carbon dioxide is carried through the blood via hemoglobin in the red blood cells to be released in the lung (Lieseke. 2012).

Unlike many other cells, mature red blood cells have no nuclei in humans and thus have a very flexible shape also limits the life of the cells. The red blood cell survives only an average 120 days. In time, the membrane of the red blood cells becomes easily vulnerable and they are removed from the circulation by reticuloendothelial system macrophages mostly in the spleen. After phagocytosis, the hemoglobin is exposed .Macrophages remove the iron from hemoglobin for reutilization. Iron is bound to transferring in the blood. The remaining parts of the hemoglobin are converted to bilirubin and given to the blood and then excreted into the bile by the liver. (Anil Tombak. 2019)

There are more than 300 known red blood cell (RBC) antigens and that differ between individuals. Sensitisation to antigens is a serious complication that can occur in prenatal medicine and after blood transfusion, particularly for patients who require multiple transfusions. Although pre-transfusion compatibility testing largely relies on serological methods. Typing for ABO and Rh—the most important blood groups (Lane. 2018).

2.6.3. Thrombocytes (Platelet)

Thrombocytes, or platelets, are spherical or ovoid cell fragments which are 0.5 to 3 microns in diameter. There are normally 150,000 to 450,000 platelets per millimeter of blood. 'Platelets are cytoplasmic fragments of large bone marrow cells called megakaryocytes. The typical platelet life span is 8 to 10 days. Platelets actively participate in hemostasis (the stoppage of bleeding or of circulation). Platelets prevent blood loss and have three functions that begin the clotting process (Lieseke.2012).

2.6.3.1. Thrombocytopenia in Chronic Liver Disease

Thrombocytopenia is a common haematological complication in patients with chronic liver disease (CLD), and is generally defined as any decrease in platelet count below the lower normal limit (<150 000/μL, with subdefinitions 50-100 000/μL [moderate] and <50 000/μL [severe]) (Peck-Radosavljevic.2017).

2.6.3.2. Causes of Thrombocytopenia in CLD

Thrombocytopenia in CLD is always linked to cirrhosis, except in a few cases of HCV infection. Multiple pathophysiological mechanisms are responsible and more than one mechanism at a time may account for decreased platelet counts. Decreased levels/activity of the haematopoietic growth factor TPO, hepatic carcinoma, chemotherapy, and bone marrow inhibition by excessive alcohol ingestion, hypersplenism secondary to portal hypertension, antiplatelet antibodies and antiviral treatment-induced myelosuppression may all contribute to the development of thrombocytopenia in CLD The major mechanisms for thrombocytopenia in cirrhosis are decreased production of TPO in the liver and splenic platelet sequestration (Peck-Radosavljevic.2017).

2.7. Complete Blood Count (CBC)

A complete blood count (CBC) provides physicians and other health-care professionals with an overview of cells and cell fragments in the circulating blood. The amounts of different types of cells in the specimen as well as physical characteristics of these cells are

included in the CBC results. Used alone or along with other diagnostic laboratory tests, the CBC helps the physician diagnose disorders follow the course of treatment, and determine prognoses (Lieseke, 2012).

2.8. Manual Blood Cell Counts

Red blood cells, white blood cells, and platelets may be counted manually by a qualified laboratory professional, blood samples are mixed with a specified amount of diluents and added to a hemocytometer. The hemocytonneter is a chamber of specific dimension and depth that has a grid marked for counting the cells under the microscope. The cells are counted using the magnification of the microscope. Because of the standardized dilution ratio and dimensions of the hemocytometer, a mathematical calculation is used to determine the number of cells in a milliliter of blood (Lieseke, 2012).

2.9. Automated analyzer for complete blood counting testing

Blood cell analyzers have come into use with advances in technology. In hospitals and reference laboratories these analyzers allow for large volumes of tests to be performed in a short period of time. Most of these test procedures use electrical impedance (a process for counting blood cells that depends on their resistance to the flow of an electrical current and differentiate blood cells. Beckman-Coulter, Abbott, ABX, and Bayer-Technician are companies that produce these automated analyzers for large-scale, time-efficient hematology testing (Lieseke, 2012).

2.10. Previous studies

In the case-control study, done in Iraq, samples are collected from seventy-five patients with hepatitis. Hematological analysis showed increase level of WBC in patients with HAV, HBV and HCV compared to a low level of these markers healthy control, while there are low levels of PLT, HB and PCV in patients compared to a high level of these markers in healthy control. However, the significant association ($p<0.05$) have appeared between hepatitis infection and each of WBC and PLT. Showed the highest level of PLT and WBC seemed in patients with HCV, whereas the highest level of PCV detected in patients with HAV On the other hand, the highest level of HB observed in patients with HBV. (TURKI, *et al*.2020)

A previous study done in Hospital of Lanzhou University (Lanzhou, China) in 1,597 patients with chronic HBV infection at the First, who met the inclusion criterion of positive serum HBV surface antigen (HBsAg) for >6 months, were enrolled between June 2016 and August 2017. Platelet count significant decreased ($P<0.00$). (Yang, Ya-Ting, *et al*.2020).

A previous study in a total of 1,048 patients with liver-biopsy-confirmed NAFLD seen between 2002 and 2008 were enrolled from nine hepatology centers in Japan. Laboratory evaluations were performed for all patients. A linear decrease of the platelet count with increasing histological severity of hepatic fibrosis was revealed. (Yoneda, Masato, *et al*.2011)

A previous study in North Bihar (India) was conducted on 50 patients to assess the hematological abnormalities and haemostatic derangements in CLD patients to reduce the morbidity. Broadly, the hematological abnormalities are viewed under abnormalities in RBCS, WBCS, platelets and coagulation profile, Various hematological abnormalities encountered were normocytic, normochromic anemia, macrocytic mostly in alcholics, leukocytosis was more compared to leucopenia and thrombocytopenia, increased prothrombin time and APTT (Jha&Kumar, 2019).

A previous study done to investigate the changes in red blood cell count in patients with different liver diseases and the correlation between red blood cell count and degree of liver damage. The clinical data of 1427 patients with primary liver cancer, 172 patients with liver cirrhosis, and 185 patients with hepatitis.Red blood cell count showed significant

differences between patients with chronic hepatitis, liver cancer, and liver cirrhosis and were highest in patients with chronic hepatitis and lowest in patients with liver cirrhosis ($P < 0.05$). For patients with liver cirrhosis, red blood cell count can reflect the degree of liver damage, which may contribute to an improved liver function prediction model for these patients (Zhonghua. 2016).

In previous study done in 98 Patients with NAFLD found lower platelet count and higher MPV, PCT, and PDW compared to the controls ($P < 0.05$) (Milovanovic Alempijevic T,*etal.* 2017).

A previous study found significant decrease in PCT in comparison to controls were noted in examined ALC ($p < 0.00$) and NAFLD ($p < 0.01$). Decreased level of MPV was observed in NAFLD group (, $p < 0.00$). Additionally, PCT correlated with NFS ($p < 0.00$). Evaluated PLT indices correlated with MELD score (MPV, $p < 0.00$; PCT, $p < 0.05$) (Michalak ,*et al*., 2021).

In a prospective observational study which spectrum of various hematological indices and complications of alcoholic liver disease were observed in 88 patients from 2013-14 who were admitted in department of general medicine, PGIMS, Rohtak. The relationship between the MELD score group and the hemoglobin was statistically significant with *p value* of <0.01 and the variation of thrombocytopenia among different groups was statistically significant with *p value* of <0.01 (Jain D. *et al*.2016).

In prospective study done in Mexico in 123 consecutive patients with NAFLD without cirrhosis.Individuals were prospectively included in the study after February 2018. The presence of NAFLD thrombocytopenia was identified in 20 (16%), whereas neutropenia was identified in 9 (7%). In the subset of 20 patients with NAFLD and thrombocytopenia, granulocytopenia was identified in 5 (25%), whereas in the subset of 9 patients with granulocytopenia, thrombocytopenia was identified in 5 (55%). We found a significant association between thrombocytopenia and both leukopenia and granulocytopenia ($p = 0.004$) (Rivera., *et al*.2021).

A previous study done in 117 children with ultrasound evidence of NAFLD undergoing liver biopsy for diagnosis of nonalcoholic steatohepatitis (NASH), were prospectively enrolled between January 2011 and May 2013 in the setting of a tertiary care center, were studied, hematological components: red cell count, Hb, hematocrit, and RDW values were

all significantly higher in NASH group compared with NAFLD group ($P < 0.05$ for each parameter) (Giorgio, *et al*.2017).

Previous studies included 3272 HBV-infected patients and 2209 healthy controls. Chronic hepatitis B (CHB) patients had significantly increased RDW levels compared with healthy controls ($p < 0.001$). Moreover, acute on chronic liver failure (ACLF) patients ($p < 0.001$) and cirrhotic patients ($p < 0.001$) had significantly elevated RDW levels compared with CHB patients. However, no statistical significance was obtained in RDW levels between cirrhosis and ACLF ($p = 0.051$) (Fan, *et al*.2018).

CHAPTER III

Materials and methods

3.1. Study design

This is a case control study

3.2. Study area

Conducted in Khartoum state in the period between October 2019 and February 2021.

3.3. Study population

A total 100 participant where recruited to this study fifty were liver disease patient, remaining participants were healthy appearing as control group.

3.4. Inclusion Criteria

This study included patient diagnosed with liver disease hepatitis B, hepatitis C and liver Cirrhosis as cases and other participant healthy appearing as control group.

3.5. Exclusion Criteria

Any participant has a diseases rather than chronic liver disease an effect on blood cells are excluded.

3.6. Ethical consideration

Procedure of whole blood sampling was explained to the participant. All participants were informed verbally about research objectives and procedures during the interview period.

3.7. Data collection tools

The primarily was collected by using a pre design questionnaire.

3.8. Blood sampling

Tow fifty ml of EDTA venous blood was taken, samples then taken carefully within 4 hours to Ibn-hisham health Center in Omdurman althawrah neighborhood for analysis.

3.9. Methods of analyzer

Venous blood EDTA well mixed put in probe of machine and press start, printer result is obtained in few seconds.

3.10. Procedure of analyzer

The Sysmex XP-300 is hematology automated analyzer three differential used quickly perform full blood counts and it made by Sysmex corporation principles of measurement (Japan).

Diluted blood is pass through a tube witch thin enough that can pass cells by one at a

time, characteristic about the cell are measured using lasers or electrical impedance. The cells pass through an opening with an electrical current flowing through it. The changes of electrical resistance due to the formed elements in the sample are monitored and they are counted as voltage pulses. These pulses are proportional in height to the volume of the cells, which allows them to be identified as white blood cells, red blood cells, or platelets.

3.11. Quality control

All quality control measures were adopted during specimen collection and processing. Complete Blood Count (CBC) protocol is a standard blood panel from the *National Health and Nutrition Examination Survey (NHANES)*

Blood is collected from standard venipuncture in a 3 r 4 ml K3 EDTA tube. The ambient blood sample is placed into a hematological analyzer for CBC and differential analyses (sysmex xp-300). The blood tested within six hours after venipuncture, samples run after accepted result of control for the sysmex instrument.

3.12. Data analysis

The data was analyzing using statistical analysis performed with statistical Package for Social sciences (SPSS) software version 16. To compare means and standard deviation of hematological values, only $P<0.05$ or less were considered significant

CHAPTER IV

Results

4.1 General characteristics of the study population

Th4is study is conduct on 100 subjects, 64 (64%) are males, 29 of them has chronic liver disease and remnant are healthy and 36 (36%) are females, 21 are chronic liver disease and 15 are healthy {Table and Figure 4-1}.

The study was conducted on 50 patients suffering from chronic liver disease, where the frequency of the disease type showed that hepatitis B (HBV) is more prevalent, accounting for 50%, then hepatitis C (HCV) represents 34% and cirrhosis (CIRR) represents 16%.{ Figure 4-1}.

Table 4-1: frequency of gender among study population.

Gender	Cases	control
Male	29	35
Female	21	15
Total	50	50

4.2 The results of CBC analysis

The results of WBC obtained in this study give Mean ± SD= (7.07 ± 3.74) in case group while in control group = (6.85 ± 1.37) and P-value=0.66 that means no statistically significant change between two groups in WBC. {Table4-4}

Table 4-2: Mean ± SD of WBC among case and control

Variables	Case	Control	P- *value*
WBC	50	50	0.66
	7.07 ± 3.74	6.85 ± 1.37	

In RBC case group Mean ± SD= (3.14 ± 0.60) while in control group = (4.85 ± 0.42) and (*P.value*=0.00). That means statistically significant different.

In HGB case group Mean ± SD = (9.13 ± 1.75) while in control group = (14.01 ± 1.09) and (*P.value*=0.00). That means statistically significant different.

In HCT case group Mean ± SD = (27.85 ± 5.02) while in control group = (41.87 ± 3.27)

and (*P.value*=0.00). That means statistically significant change.

In MCV case group Mean ± SD = (89.02 ± 5.41), while in control group = (86.16 ± 2.86), and (*P.value*=0.00). That means statistically significant different

In MCH case group Mean ± SD = (29.11 ± 2.13), while in control group = (28.85 ± 1.10), and (*P.value*=0.44). That means no statistically significant change.

In MCHC case group Mean ± SD = (32.49 ± 2.15), while in control group = (33.47 ± 0.85), and (*P.value*=0.00). That means statistically significant different.

{Table 4-3}.

Table4-3: Mean ± SD of RBC, HBG, HCT, MCV, MCH, MCHC.

Variables	Case	Control	P- *value*
RBC	Mean ± SD 3.14 ± 0.60	Mean ± SD 4.85 ± 0.42	0.00
HBG	Mean ± SD 9.13 ± 1.75	Mean ± SD 14.01 ± 1.09	0.00
HCT	Mean ± SD 27.85 ± 5.02	Mean ± SD 41.87 ± 3.27	0.00
MCV	Mean ± SD 89.02 ± 5.41	Mean ± SD 86.16 ± 2.86	0.00
MCH	Mean ± SD 29.11 ± 2.13	Mean ± SD 28.85 ± 1.10	0.44
MCHC	Mean ± SD 32.49 ± 2.15	Mean ± SD 33.47 ± 0.85	0.00

In PLT case group Mean ± SD = (1.37 ± 5.15), while in control group = (2.67 ± 5.88), and (*P.value*=0.00). That means statistically significant different.

In MPV case group Mean ± SD = (9.99 ± 1.25),while in control group = (9.76 ± 1.05), and (*P.value*=0.33). That means statistically no significant different.

In PCT case group Mean ± SD = (137 ± 5.15), while in control group = (267 ± 5.88), and (*P.value*=0.00). That means statistically significant different.

{Table 4-6}.

Table 4-4: Mean ± SD of PLT, MPV and PCT.

Variables	Case	Control	P- *value*
PLT	Mean ± SD 1.37 ± 5.15	Mean ± SD 2.67 ± 5.88	0.00
MPV	Mean ± SD 9.99 ± 1.25	Mean ± SD 9.76 ± 1.05	0.33
PCT	Mean ± SD 0.14 ± 0.05	Mean ± SD 0.26 ± 0.05	0.00

Table 4-5: significant difference of CBC among type of disease

Variables	Type of Disease	N	Mean	*P- value*
WBC	HBV	25	8.15	0.10
	CIRR	8	5.34	
	HCV	17	6.29	
RBC	HBV	25	3.42	0.00
	CIRR	8	2.47	
	HCV	17	3.05	
HBG	HBV	25	9.93	0.00
	CIRR	8	7.25	
	HCV	17	8.84	
HCT	HBV	25	30.12	0.00
	CIRR	8	22.69	
	HCV	17	26.95	
MCV	HBV	25	88.52	0.25
	CIRR	8	91.91	
	HCV	17	88.38	
MCH	HBV	25	29.17	0.91
	CIRR	8	29.28	
	HCV	17	28.94	
MCHC	HBV	25	32.60	0.58
	CIRR	8	31.76	
	HCV	17	32.67	
PLT	HBV	25	172.56	0.00
	CIRR	8	86.88	
	HCV	17	108.88	
MPV	HBV	25	10.06	0.76
	CIRR	8	10.14	
	HCV	17	9.81	
PCT	HBV	25	0.17	0.00
	CIRR	8	0.10	
	HCV	17	0.11	

CHAPTER V

Discussion, conclusion and recommendations

5.1. Discussion

This study showed decreased significant association in hemoglobin, PCV and platelets count in patients with HBV, HCV and liver cirrhosis compared to healthy control (*P-value* 0.00), this in line with previous a case control study, done in Iraq, in patients with hepatitis(HAV, HBV and HCV). Hematological analysis showed low levels of PLT, HB and PCV in patients compared to a high level of these markers in healthy control, the significant association ($p<0.05$). (JALIL, *et al*.2020). Whereas in same previous study showed increase level of WBC in patients with HAV, HBV and HCV compared to a low level of these markers healthy control, while current study not found statically significant difference between patients with HBV, HCV and liver cirrhosis compared to healthy appear control (*P-value* 0.66).

Current study found decreased significant association in red blood cells count and hematocrit in case group with HBV, HCV and liver cirrhosis compared to healthy control group (*P-value* 0.00), also agreement with previous prospectively study enrolled between January 2011 and May 2013 in the setting of a tertiary care center, NAFLD undergoing liver biopsy for diagnosis of nonalcoholic steatohepatitis (NASH), 41 NAFLD) and 76 NASH children were studied, hematological components: red cell count, Hb, hematocrit, and RDW values were all significantly lower in NAFLD group compared with NASH group ($P < 0.05$ for each parameter). (Giorgio, Valentina, *et al*.2017).

In this study the mean corpuscular volume of red blood cells among cases which reflect normocytic anaemia. Note the gradient highest in patient with cirrhosis, then HBV, and less one HCV, the result showed increased different significant in MCV between case and control group (*p-value*=0.00). But there is no statistically significant difference in MCV between the types of chronic liver disease in this study (*p-value*=0.25).

This study did not show a difference between case and control group in mean corpuscular hemoglobin (MCH) which *(p value*=0.44) that means normochromic cells. This in line with retrospective study conducted in Medical University of the Vienna between August 2007 and December 2015, studying red blood cell indices in patients with chronic liver disease, (n = 253) 78% had normocytic anemia with($P < 0.34$). (Scheiner *et al*, 2019).

This study did not show a statistically significant difference in mean corpocsular hemoglobin concentration (MCHC), between case and control group.

Current study showed significant decrease of platelet count between case and control group (*P-value*=0.00), also matching to previous study done in the First Hospital of Lanzhou University (Lanzhou, China), enrolled between June 2016 and August 2017, which platelet count significant decreased (P<0.001).(Yang, 2020).

However this study showed a statistically significant decrease in platletcrit (PCT) between case and control group, this reflects the effect of chronic liver disease on platelet counts and plateletcrit, which (*P-value*=0.00) for platelet count and platletcrit.

This study did not show a statistically significant difference in (MPV), between case and control group, this may reflect the lack of influence of chronic liver disease on the mean platelet volume.

In the present study showed no statistically insignificant in the white blood cells count and chronic liver of disease (*P-value*=0.66), which not matched with previous study done in North Bihar- India, was increased statistically significant different between chronic liver disease and white blood cells count. (Sudhir, *et a.l*2019).

In deep details about the association between the types of chronic liver disease among the patients studied, this study was found that the patients with cirrhosis had the lowest average red blood cell counts, then HBV and HCV, respectively. This is in line with a previous study conducted in China where it found that red blood cell count showed significant differences between patients with chronic hepatitis, liver cancer, and liver cirrhosis and was highest in patients with chronic hepatitis and lowest in patients with liver cirrhosis ($P < 0.05$). For patients with liver cirrhosis, red blood cell count can reflect the degree of liver damage, which may contribute to an improved liver function prediction model for these patients. (Zhonghua, 2016).

5.2. Conclusion

This study concluded that chronic liver disease has an effect on red blood cells, hemoglobin, hematocrit, platelet count, plateletcrit, MCV and MCHC.

No difference on WBC, MCH, MPV.

5.3. Recommendations

On bases of results obtained in this study it is recommended do CBC as routine test for

patient with chronic liver disease.

Other Cohort studies can be done to asses' effect duration of chronic liver disease on CBC.

Further studies should be done with larger sample size.

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Appendices

Appendix I

Questionnaire

Sudan University of Sciences and Technology

College of Graduate Studies

Determination of Complete Blood Count among Chronic Liver Disease - Ibn Sina Hospital-Sudan

قياس تعداد الدم الكامل وسط مرضى الكبد المزمن - مستشفى ابن سينا -السودان

Serial No (….)

Demographical data:

-Age.....Years.

-Gender: Male (...) Female (....)

-Diagnosis.....

Laboratory Results:

Complete Blood Count parameters:

-TWBCs.....

-RBCs.....

-Hb.....

-HCT.....

-MCV.....

-MCH.....

-MCHC.....

-PLT.....

-MPV.....

-PCT.....

Appendix II

Hematology analyzer, sysmex XP-300