Liver pathophysiology and liver disease markers

The liver is the largest glandular organ present in vertebrates and some other animals. It is reddish brown in colour with four lobes of unequal size and shape (Fig. 1. 0). It is located at the right side of the abdominal cavity beneath the diaphragm.

The liver has a wide range of functions. It would be difficult to overestimate the its importance to the healthy functioning of the human body. It acts as a giant chemical processing plant , a battery, a filter, a warehouse and distribution centre.. The chemical reactions, called metabolism, are central in the regulation of body homeostasis. The liver is able to carry out its functions through the help of liver cells called hepatocytes (Ramaori, et al., 2008). These cells contain essential enzymes that perform the vital metabolic functions.

The liver metabolises both beneficial and harmful substances. It stores nutrients and other useful substances, as well as detoxifying or breaking down harmful compounds. These can be then excreted from the body in bile via the liver; in urine via the kidney, or by other means. These cells are described as supermodels in the world of cellular metabolism.

In summary, the liver performs the following functions:

- Metabolism of fats, proteins, and carbohydrates
- Excretion of bilirubin, cholesterol, hormones, and drugs
- Storage of glycogen, vitamins, and minerals
- Bile production and excretion
- Blood detoxification and purification
- Enzyme activation

- Synthesis of plasma proteins, such as albumin and globulin, and clotting factors

Pathophysiology of the Liver

The functions of the liver described above occur in the normal functioning of the liver but in some cases ther are abnormal functioning of the liver due to disease conditions which can result from a wide variety of insults, including infections, drugs, toxins, ischemia, and autoimmune disorders.

Abnormalities of liver function can be divided broadly into two groups:

- those caused by a malfunction of the liver cells (such as cirrhosis or hepatitis)
- those caused by an obstruction of the biliary tract (such as bile duct stones or cancer of bile duct and haemocytes).

Most liver disorders cause some degree of hepatocellular injury and necrosis, resulting in various abnormal laboratory test results and, sometimes, symptomssuch as jaundice , acute GI bleeding . Some of the diseases lead to by impairment of biliary secretion; and cryptogenic cirrhosis, by liver fibrosis and resultant portal venous hypertension).

The diagnosis of the diseases and the general state of the liver is made by blood tests. These tests help to pinpoint the extent of liver damage. One of these blood tests is called Liver function tests.

Liver function tests.

As the immune system, digestive tract, kidney, brain and cardio-vascular system all depend on a healthy and well-functioning liver, there is great need

to know the state of the liver and also to know some of the key liver disease markers for effective management of this vital organ. The diagnosis of liver function is made by blood tests. The liver makes a number of chemicals when playing its vital roles. The blood levels of these chemicals are altered by various liver disorders as they pass into the bile and the bloodstream. One of the tests used for the measurement of these chemicals in the blood sample is called Liver function tests which assess the general state of the liver and bilarry system. It involves the measurement of bilirubin, a compound formed by the catabolism of hemoglobin; ammonia, a product of protein catabolism that is normally converted into urea by the liver before being excreted by the kidneys; proteins that are made by the liver including total protein, albumin, prothrombin, and fibrinogen; cholesterol and triglycerides, which are made and excreted via the liver; and the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and lactate dehydrogenase (LDH). Other liver function tests include serological (tests to demonstrate antibodies) and DNA tests for hepatitis and other viruses, tests for antimitochondrial and smooth muscle antibodies, transthyretin (prealbumin), protein electrophoresis, bile acids, alpha-fetoprotein, and a constellation of other enzymes that help differentiate necrotic versus obstructive liver disease.

Key liver disease markers and how they aid diagnosis.

Laboratory tests for total protein, albumin, ammonia, transthyretin, and cholesterol are markers for the synthetic function of the liver. Tests for cholesterol, bilirubin, ALP, and bile salts are measures of the secretory

function of the liver. The enzymes ALT, AST, GGT, LD, and tests for viruses are markers for liver injury.

Some liver function tests are used to determine if the liver has been damaged or its function impaired. Elevations of these markers for liver injury or disease tell the physician that something is wrong with the liver. ALT and bilirubin are the two primary tests used largely for this purpose. Bilirubin is measured by two tests, called total and direct bilirubin. The total bilirubin measures both conjugated and unconjugated bilirubin while direct bilirubin measures only the conjugated bilirubin fraction in the blood. Unconjugated bilirubin is formed from heme in the reticuloendothelial cells in the spleen that remove old red blood cells from the circulation. The RE cells release the bilirubin into the blood where it is bound by albumin and transported to the liver. The bilirubin is taken up by liver cells and conjugated to glucuronic acid, which makes the bilirubin water soluble. This form will react directly with a Ehrlich’s diazo reagent, hence the name direct bilirubin. While total bilirubin is elevated in various liver diseases, it is also increased in certain anemias caused by increased red blood cell turnover. Neonatal hyperbilirubinemia is a condition caused by an immature liver than cannot conjugate the bilirubin. The level of total bilirubin in the blood becomes elevated, and must be monitored closely in order to prevent damage to the brain caused by unconjugated bilirubin, which has a high affinity for brain tissue.. Direct bilirubin is formed only by the liver, and therefore, it is specific for hepatic or biliary disease. Its concentration in the blood is very low and therefore, even slight increases are significant. Highest levels of direct bilirubin are seen in obstructive liver diseases. However, direct biliruibn is

not sensitive to all forms of liver disease (e. g., focal intrahepatic obstruction) and is not always elevated in the earliest stages of disease, and therefore, ALT is needed to exclude a diagnosis.

ALT is an enzyme that transfers an amino group from the amino acid alanine to a ketoacid acceptor.. Although ALT is present in other tissues besides liver, its concentration in liver is far greater than any other tissue, and blood levels in nonhepatic conditions rarely produce levels of a magnitude seen in liver disease. The enzyme is very sensitive to necrotic or inflammatory liver injury. Consequently, if ALT or direct bilirubin are increased, then some form of liver disease is likely. If both are normal, then liver disease is unlikely.

These two tests along with others are used to help determine what is wrong. The most useful tests for this purpose are the liver function enzymes and the ratio of direct to total bilirubin. These tests are used to differentiate diseases characterized primarily by hepatocellular damage (necrosis) from those characterized by obstructive damage. In hepatocellular damage, the transaminases, ALT and AST, are increased to a greater extent than alkaline phosphatase. This includes viral hepatitis, which gives the greatest increase in transaminases (10-50 fold normal), hepatitis induced by drugs or poisons (toxic hepatitis), alcoholic hepatitis, hypoxic necrosis (a consequence of congestive heart failure), chronic hepatitis, and cirrhosis of the liver.

Aspartate aminotransferase is not as specific for liver disease as is ALT, which is increased in myocardial infarction, pancreatitis, muscle wasting diseases, and many other conditions(Hannah, 2007). However, differentiation of acute and chronic forms of hepatocellular injury are aided

by examining the ratio of ALT to AST, called the DeRitis ratio. In acute hepatitis, Reye’s syndrome, and infectious mononucleosis the ALT predominates. However, in alcoholic liver disease, chronic hepatitis, and cirrhosis the AST predominates.

Alkaline phosphatase is increased in obstructive liver diseases, but it is not specific for the liver. Increases of a similar magnitude (three-to five-fold normal) are commonly seen in bone diseases, late pregnancy, leukemia, and some other malignancies. The enzyme gamma-glutamyl transferase (GGT) is used to help differentiate the source of an elevated ALP. GGT is greatly increased in bstructive jaundice, alcoholic liver disease, and hepatic cancer..

Some liver function tests are not sensitive enough to be used for diagnostic purposes, but are elevated in severe or chronic liver diseases. These tests are used primarily to indicate the extent of damage to the liver. Tests falling into this category are ammonia, total protein, albumin, cholesterol, transthyretin, fibrinogen, and the prothrombin time.

Conclusions

Liver function tests done individually do not give the physician very much information, but used in combination along with a careful history, physical examination, and imaging studies they contribute to making an accurate diagnosis of the specific liver disorder. Different tests will show abnormalities in response to liver inflammation, liver injury due to drugs, alcohol, toxins or viruses, liver malfunction due to blockage of the flow of bile, and liver cancers.