HEPATIC MANIFESTATIONS OF ACUTE & CHRONIC ENTERIC FEVER

THESIS

Submitted by

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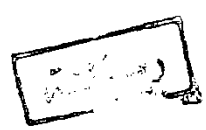

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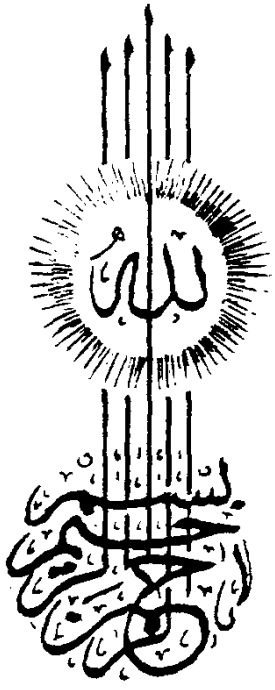

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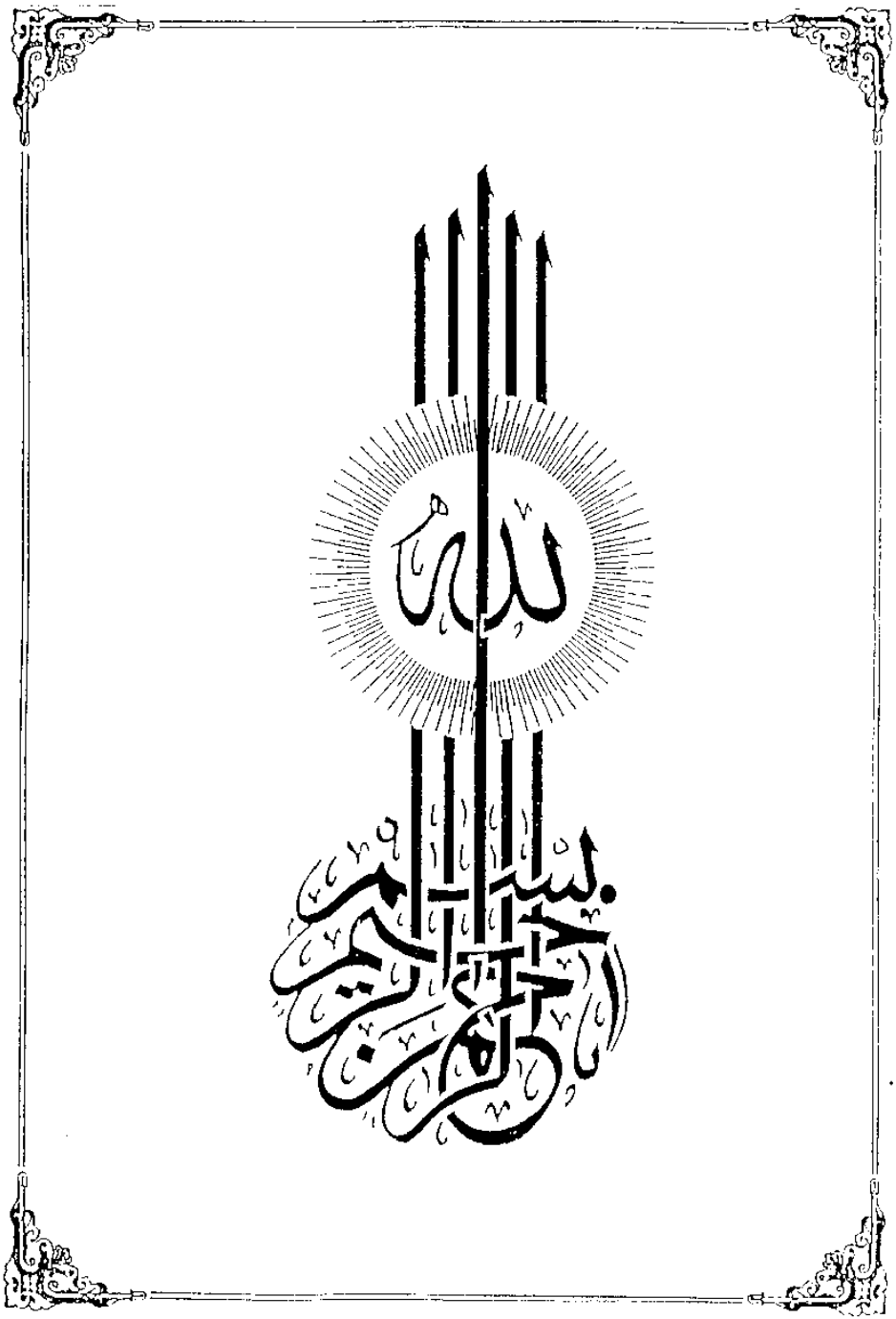

ACKNOWLEDGEMENT

This thesis has been performed in Abbassia Fever Hospital, Cairo, the biggest fever hospital in the Middle East comprising 1500 beds.

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Lastly and not least, I hope that this five years study on the subject of salmonellosis with great stress on the Egyptian experience past and present from the clinical and laboratory point of view, will lighten the way to my collegues in the Fever hospitals all over Egypt working in localities where bilharziasis and salmonellosis are the most important endemic disease and where laboratory facilities are simple.

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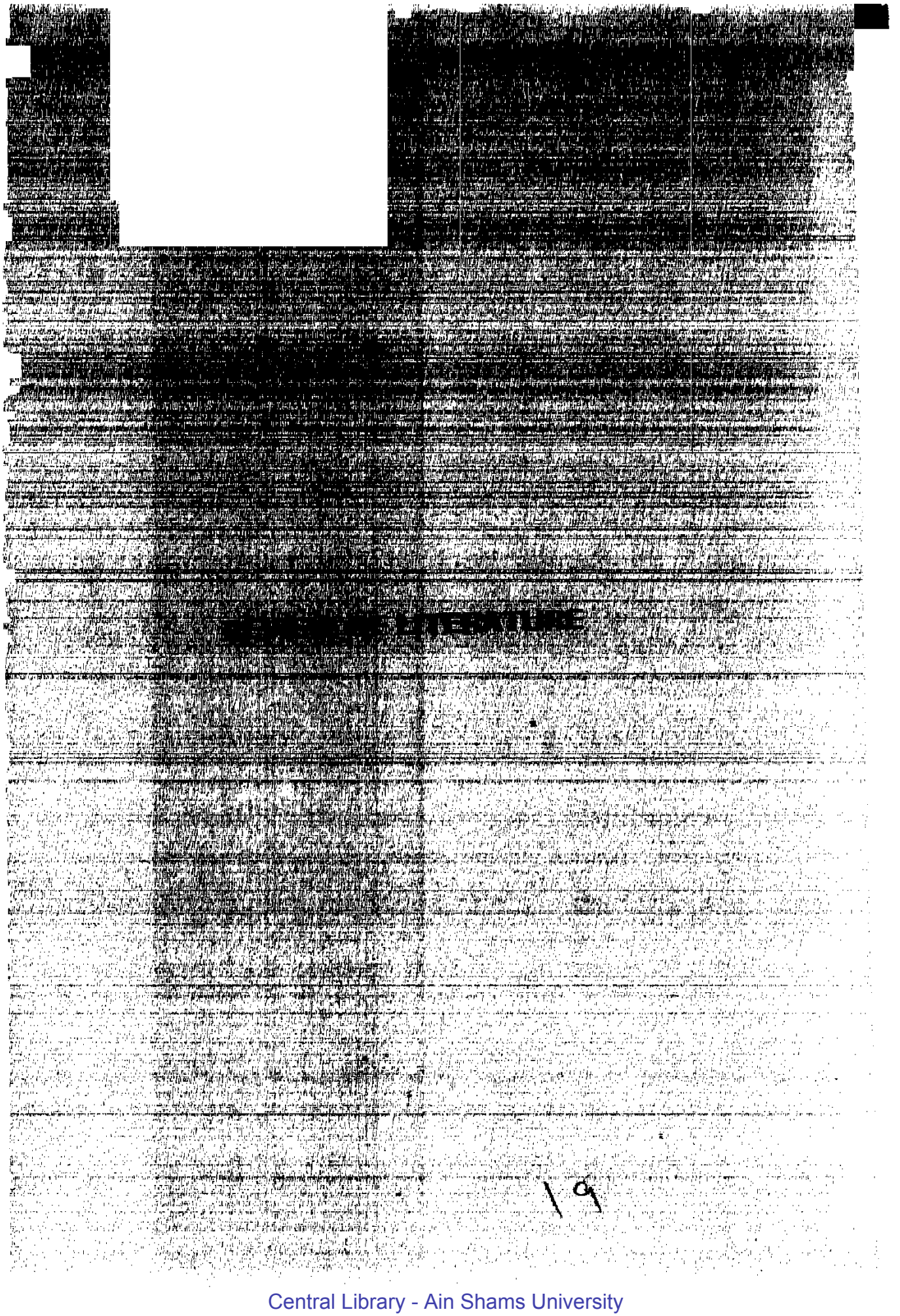
INTRODUCTION

INTRODUCTION AND AIM OF THE WORK

Acute enteric fevers are endemosporadic in Egypt. The average number of reported cases of enteric fever per year is 15000 (El-Akkad 1970). This reported number is far below the real one as many cases of enteric fevers are treated in the private practice without notification. Chronic salmonellosis present a clinical entity of salmonella infection quite different from classical enteric fever characterized by prolonged fever and bacteremia in bilharzial patients.

Enteric fever involves almost all the major organs of the body and is known to produce either toxic or diffuse parenchymatous degenerations (Khosla 1981). Mallory 1898 described focal areas of necrosis as a postmortem findings in the liver of typhoid patients. Stuart and Pullen 1946 observed typhoid hepatitis in typhoid cases. Assif et al., 1969 described typhoid hepatitis as enlargement of the liver, abnormal liver function tests and elevated serum transaminases without jaundice. Ramachandran et al., 1974 reported hepatomegaly in about one fourth of patients of enteric fever. Abdel Wahab et al.,1977 reported hepatomegaly in 34% of acute enteric fever in Egypt.

The aim of this work is to study the hepatic manifestations of acute and chronic enteric fevers from the clinical, biochemical and pathological point of view in an attempt to elucidate the insult of acute and chronic enteric fevers on the liver.



ANATOMY OF LIVER

The liver is the largest organ in the body weighing 1200-1500 grams comprising one fifth of the total adult body weight. Sheltered by the ribs in the right upper quadrant, it is shaped like a pyramid whose apex reaches the xiphisternum. The upper border lies approximately at the level of the nipples. There are 2 anatomical lobes, the right being about 6 times the size of the left. The liver had a double blood supply, the portal vein brings venous blood from the intestines and the spleen and the hepatic artery coming from the coeliac axis, supplies the liver with arterial blood. The venous drainage from the liver is into the right and left hepatic veins which emerge from the back of the liver and at once enter the inferior vena cava (Sherlock 1981).

As regards the surface markings of the liver, the upper border of the right lobe is on a level with the 5th rib at a point 2 cm medial to the right mid clavicular line. The upper border of the left lobe corresponds to the upper border of the 6th rib at a point in the left midclavicular line. The lower border passes obliquely upwards from the 9th right to the 8th left costal cartilage. In the right midclavicular line, it lies between a point just under to 2 cm below the costal margin. It crosses mid line about mid way between the base of the xiphoid and the umbilicus and the left lobe extends only 5 cm to the left of the sternum (Sherlock 1981).

LIVER FUNCTION TESTS

Biochemical methods in patients with liver disease are needed for accurate diagnosis, to estimate the severity, to assess prognosis and to evaluate therapy (Sherlock 1981).

Tests most useful in the diagnosis of jaundice are the serum alkaline phosphatase level, electrophoresis of the serum proteins and serum transaminase values. Daily inspection of stools is useful. An isolated rise in serum unconjugated bilirubin suggests Gilbert's syndrome or haemolysis.

Assessment of the severity of liver cell damage is done by serial serum total bilirubin, albumin, transaminase and prothrombin after vitamin K estimations.

Schistosomal cases with hepatosplenomegaly and ascites showed increased serum bilirubin above normal level in 33.6% of the cases (Issa 1979). HBsAg was positive in 20% of schistosomal cases with raised serum bilirubin and in only 4% with normal serum bilirubin. Also most of the cases (71.7%) with positive HBs Ag had high serum bilirubin suggesting the occurrence of a sort of chronic hepatitis in these cases (Issa 1979).

The diagnosis of minimal hepatocellular damage due to well compensated cirrnosis or alcoholic liver damage may be done by noting minimally elevated serum bilirubin and serum transaminase values. Similar changes will be seen in conditions such as fever or circulatory failure. Serum Y-glutamyl

transpeptidase (Y-GT) is useful for diagnosing minimal alcoholic liver damage.

Hepatic infiltrations such as primary or secondary cancer, amyloid disease or reticuloses are suggested by an elevated serum alkaline phosphatase without jaundice.

Immunological tests are of particular value, especially the smooth muscle antibody for the diagnosis of chronic active hepatitis and the mitochondrial antibody for primary biliary cirrhosis. Specific serum markers for virus hepatitis are available. These immunological and virological tests together with the wider use of needle liver biopsy and better imaging using scanning, ultrasound, arteriography and percutaneous and endoscopic cholangiography, have made diagnosis much more precise. The diagnostic role of the standard liver function tests has therefore been reduced. They remain useful for initial screening for hepatobiliary disease, for detecting severity and for following progress.

PROTEIN METABOLISM

The human liver synthesizes albumin, fibrinogen, prothrombin, haptoglobin, glycoprotein, transferrin and ceruloplasmin. The immunoglobulins are synthesized by immunocytes. Normals make about 10 gms albumin daily. About 2 gms fibrinogen and

1 gm transferrin are also produced. The normal half life of serum albumin is 20-26 days. In cirrhosis, it is increased and albumin turnover is correspondlingly decreased, reflecting impaired synthesis. A rise or fall in plasma protein concentration may reflect changes not only in hepatic production but also in plasma volume (Sherlock 1981).

Serum protein changes are slow and do not immediately reflect acute liver damage. Even complete cessation of albumin production results in only 25% decrease in serum levels after eight days. Patients with severe viral hepatitis may have normal serum albumin values. Fever and malnutrition will also tend to lower the serum albumin.

The characteristic change in chronic liver disease is a fall in serum albumin and a rise in globulin levels. In severe prolonged viral hepatitis and in cirrhosis, serum albumin levels bear a close relation to the clinical state and are helpful prognostically and in following treatment. Serum values may be normal in well-compensated cirrhosis and are of little value diagnostically.

Hyperglobulinaemia is a feature of acute and chronic hepatocellular disease. It reflects a reticuloendothelial reaction to antigen, largely of gut origin. Extremely high values characterize chronic active hepatitis, levels falling only in the later stages or with corticosteroid treatment.

As regards the electrophoretic pattern of serum proteins, in cirrhosis, albumin is reduced and in acute nepatitis, these changes are much less conspicious. The α_1-globulins contain glycoproteins and tend to be low in hepatocellular disease, falling in parallel with the serum albumin. An increase accompanies acute febrile illnesses and malignant disease. An absent $\alpha_1$globulin may indicate α_1 antitrypsin deficiency.

The α_2 and B globulins contain lipoproteins. In cholestasis, the increase in α_2 and B globulin components correlates with the height of serum lipids. This pattern may be useful in distinguishing biliary from non-biliary cirrhosis. High lipoprotein components strongly support a biliary etiology.

The Y-globulins rise in hepatic cirrhosis due to increased production. The Y-globulin peak in hepatocellular disease shows a wide base (polyclonal gammo-pathy) (Sherlock 1981).

As regards immunoglobulins, IgG is markedly increased in chronic active hepatitis and cryptogenic cirrhosis. There is a slow and sustained increase in viral hepatitis and is also increased in alcoholic cirrhosis. IgM is markedly increased in primary biliary cirrhosis and to a lesser extent in viral hepatitis and cirrhosis whether chronic active or cryptogenic. IgA is markedly increased in alcoholic cirrhosis and in primary biliary and cryptogenic cirrhosis. In chronic

active hepatitis and cryptogenic cirrhosis, the pattern is surprisingly similar with increases in IgG, IgM and to a lesser extent IgA. Patterns are not diagnostic of any one disease but only give suggestive evidence (Sherlock 1981).

SERUM ENZRME TESTS

These tests will usually diagnose the type of liver injury, whether hepatocellular or cholestatic but cannot be expected to diagnose one form of hepatitis from another or to determine whether cholestasis is intra or extrahepatic. The combination of a serum aspartate transaminase (SGOT) and alkaline phosphatase (with occassionally serum alanine transaminase, SGPT) will usually detect a patient with liver disease (Sherlock 1981). Glutamic oxalacetic transaminase (GOT) (Aspartate transaminase) is a mitochondrial enzyme present in large quantities in heart, liver, skeletal muscle and kidney and the serum levels of the enzyme increases whenever these tissues are acutely destroyed, presumably due to release from damaged cells. Very high values are found with hepatocellular necrosis or myocardial infarction.

Glutamic pyruvic transaminase (GPT) (Alanine transaminase) is a cytosol enzyme also present in the liver and although the absolute amount is less than GOT, a greater proportion