STUDY OF THE RELATION BETWEEN ALPHA-FETOPROTEIN AND MIXED LIVER CIRRHOSIS

THESIS

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BY

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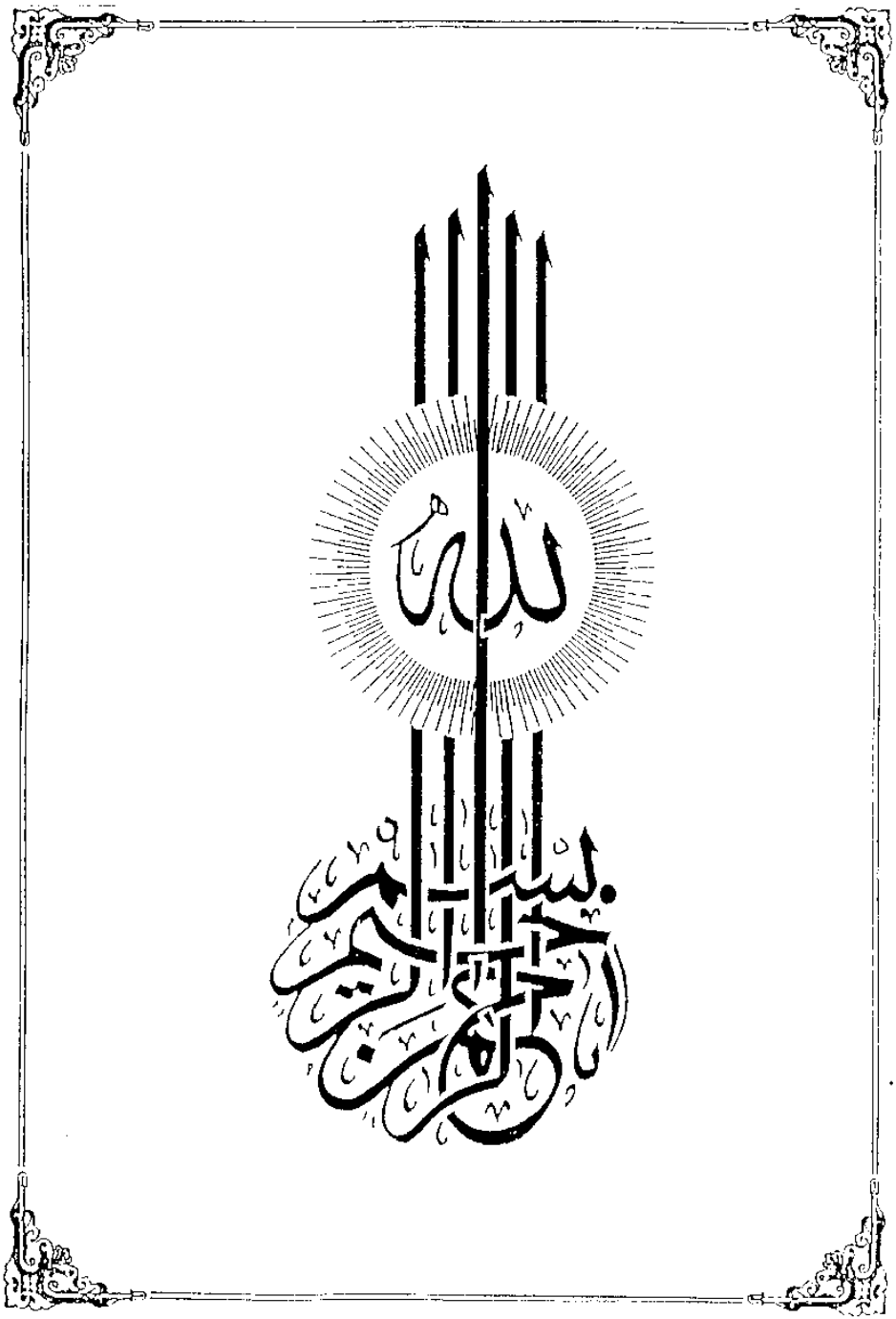

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AIM OF WORK

AFP is a normal serum protein synthesized during the fetal life (Gitlin et al, 1972).

By using the highly sensitive methods, patients with acute and chronic liver disease have shown increased values (Smith, 1971).

Human schistosomiasis headed the list of hepatic diseases in Egypt. But in bilharzial cases, other aetiological factors may be blamed and in this case, it is called mixed bilharzial fibrosis (Mousa and El-Garem,1959).

The aim of this study is to estimate the serum level of AFP in mixed liver cirrhosis and to assess the value of this test as a marker of hepatocellular regeneration.

LIVER CIRRHOSIS

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Definition:

Cirrhosis is defined anatomically as a chronic diffuse process characterized by fibrosis and nodular formation ending in disruption of the normal lobular architecture of the liver.

Functionally, the disorder is characterized by a disturbance of hepatic hemodynamics associated with a reduced functioning liver mass and with secondary alteration of extrahepatic circulation (Popper,1977).

Normal histology of the liver:

The liver is divided into lobules based on a central vein, peripheral portal tracts and between these a regular network of sinusoids. The central veins are tributaries of the hepatic veins which drain to the inferior vena cava. The portal tracts contain branches of the hepatic artery, the portal vein lymphatics and the bile ducts. The sinusoids are channels, lined by endothelial and phagocytic (Kupffer) cells, which receive blood separately from the hepatic arterial and portal venous system and convey it to the central veins. The liver cells themselves are arranged in single-cell sheets which lie between the sinusoids separating them from one another. Between the liver cells and the sinusoidal cells is the space of Disse which contains fluids draining to the lymphatics in the portal tracts. (Abdel-Hamid, 1980).

The pathogenesis and pathology of cirrhosis:

The response of the liver to necrosis is strictly limited , the most important are collapse of hepatic lobules, formation of diffuse fibrous septa and nodular regrowth of liver cells. Thus, irrespective of the aetiology, the histological pattern of the liver is the same or nearly the same (Popper, 1977).

(1) Liver cell changes:

The common initiating event in cirrhosis is liver cell necrosis. This may take the form of an acute hepatitis of viral or alcoholic type, alternatively there may be less dramatic but continuous liver cell damage as in metabolic disorders. Areas of surviving parenchyma are assumed to undergo regeneration but fail to produce normal lobular or acinar architecture, so that nodules form. The compressed necrotic zones might then form the basis of the fibrous septa of the cirrhotic liver (Gall, 1960).

In biliary cirrhosis and haemochromatosis, liver cell damage is absent or mild, the lobules remain intact and the lesion appears like that of schistosomiasis or congenital hepatic fibrosis (Gerber et al, 1973).

(2) Regeneration:

In experimental cirrhosis, regeneration of liver cells is indicated by mitotic activity (Rubin and Popper, 1967). The liver cells divide to replace lost cells, but may then continue to grow and replicate further, forming truly hyperplastic nodules. Liver cell growth occurs in waves rather than continuously, so some nodules show evidence of regeneration while others appear silent. It is therefore possible to diagnose cirrhosis in the absence of active regeneration (Phillips and Steiner, 1965).

(3) Changes in the biliary tree:

Ductular proliferation is a common finding. The biliary tree show increased branching in the terminal part and tortuosity of the smallest branches. This proliferation is almost always accompanied by inflammatory infiltration especially by neutrophil leucocytes (Masuko et al, 1964).

(4) Inflammation:

The inflammatory reaction in cirrhosis has many causes but the most important one is the injury or death of liver cells from any cause. The initiating agent such as hepatitis virus may itself stimulate a cellular response. Lymphocytes and plasma cells usually predominate in the inflammatory infiltrate, but neutrophil and eosinophil leucocytes are commonly found (Popper, 1977).

(5) Fibrosis:

Septa in a cirrhotic liver are produced by collapse of the pre-existing reticulin framework following loss of liver cells, and more important by the formation of new collagen (Popper and Udenfried , 1970). The fibrous septa may extend in bridge-like fashion joining the central vein to the portal tracts and this results in disruption of the normal lobular architecture of the liver (Yoke - Sunlee, 1982).

Classification of Cirrhosis

There are many methods of classification of liver cirrhosis but the most recent one is based on aetiology and morphology (Anthony et al,1978).

I. Morphological classification:

The subdivision of cirrhosis according to morphological characteristics should be regarded as description rather than classification for many reasons:

1) Each cirrhotic liver is unique, and its configuration is the result of the interplay of several factors. These include necrosis, regeneration fibrosis and liver cell enlargement.

2) Cirrhotic livers range from greatly enlarged organs weighing several kilograms to small shrunken livers weighing a few hundred grams. Within large or small cirrhotic livers nodule size varies widely.

3) The most important cause is the fact that cirrhosis is not a static lesion but is capable of changing its appearance in the individual patient (Scheuer, 1979).

The simplest morphological subdivision of cirrhosis is according to nodule size. By which three types are recognized.

1) Micronodular cirrhosis:

It is characterized by nodules of equal size, up to 3 mm. in diameter (Anthony et al, 1978). It is associated with thick regular septa, regenerating small nodules and by involvement of every lobule. The micronodular liver may represent impaired capacity for regrowth (Yoke-Sunlee 1982). This type corresponds to portal, Laennec's, nutritional or septal cirrhosis in older terminology (Rubin and Popper, 1967).

2) Macronodular cirrhosis:

This type corresponds to the older postnecrotic cirrhosis and to irregular or multilobular cirrhosis (Rubin and Popper, 1967).

It is characterized by the presence of nodules which are larger than those of the micronodular type and are variable in size. This type is subdivided into two categories:

- Incomplete septal cirrhosis
- Post collapse cirrhosis (Yoke-Sunlee, 1982).

3) Mixed cirrhosis:

Here the micronodular and macronodular types are present in approximately equal proportion.

Indeed, every type of cirrhosis is mixed but it is considered micro or macronodular according to whether micro or macronodules predominate (Anthony et al, 1978).

II. Aetiological classification :

A) Established aetiological association:

1. Viral hepatitis
2. Alcoholism
3. Metabolic Diseases:

   Haemochromatosis
   Wilson's disease
   α_1 - Antitrypsin deficiency
   Glycogen storage disease (types III and IV)

4. Biliary disease:

   Primary biliary cirrhosis
   Disease involving major bile ducts

5. Venous outflow obstruction

   Budd - chiari syndrome
   Veno - occlusive disease

6. Drugs and toxins
7. Intestinal by-pass for obesity
8. Others, e.g. sarcoidosis

B) Debatable aetiological factors:

1. Autoimmunity
2. Toxins
3. Parasitic disease
4. Malnutrition

C) Cirrhosis of unknown aetiology:

1. Cirrhosis without definite clinical and morphological pattern: cryptogenic cirrhosis.

2. Cirrhosis with defined clinical and morphological pattern: Indian childhood cirrhosis.

(Scheuer, 1979).