Acomparitive Study on Alpha. Feto Protein (A.F.P) in Chronic Liver Diseases

Thesis

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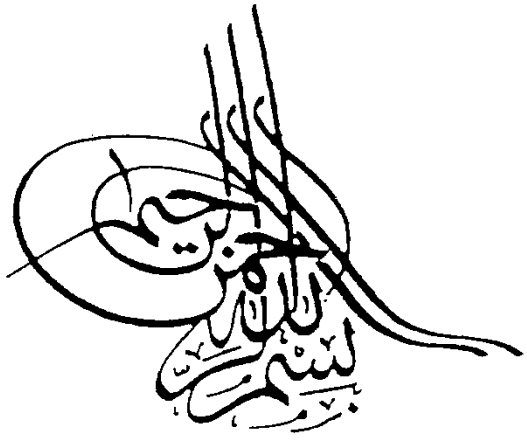

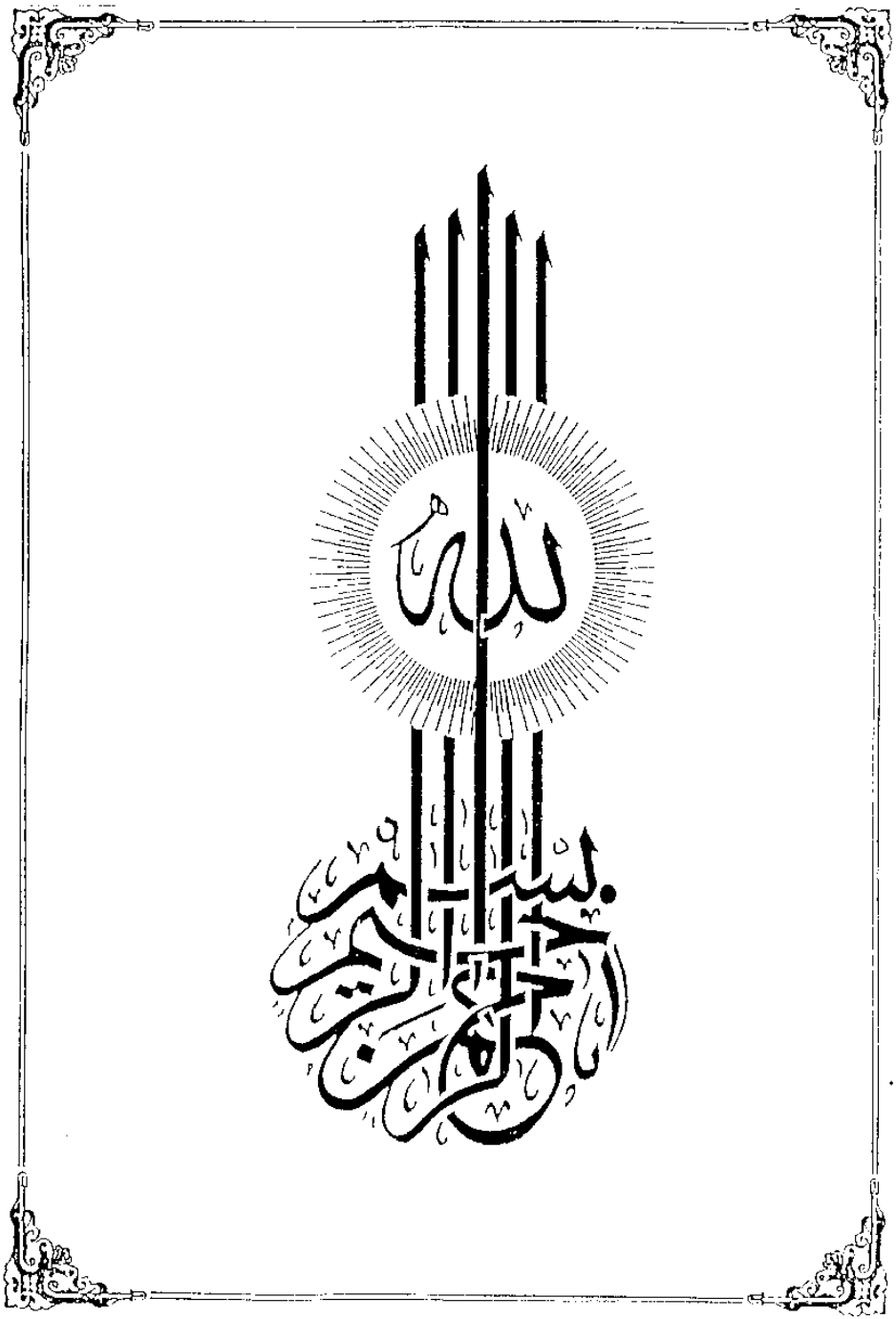

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Contents

Introduction

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Alpha -1- Feto Protein (A.F.P) was first identified in 1956 during electrophoresis experiments on plasma proteins of foetus of a few weeks old by Haibercht, Klibanski, Bergstrand and Czar as a protein which migrated between albumin and alpha -1- globulins. This protein was not initially found to be present in normal adult serum.

Interest of A.F.P. developed rapidly after the discovery by Abelev 1963 that the transplantable hepatocellular carcinoma of the mouce synthesized and secreted A.F.P. into the blood.

The association of A.F.P. with hepatoma in experimental animals raised the possibility that the presence of A.F.P. in the serum of human patients might provide a precise diagnostic test for liver carcinoma. In 1964, Tatarinov first detected A.F.P. in the serum of patients with hepatocellular carcinomas and by 1966

he has reported six such cases.

The significance of an elevated serum A.F.P concentration in the diagnosis of hepatocellular carcinoma was now soon well documented (Wepsic et al, 1979)

Increased levels (> 40 ng/ml) of A.F.P. have been demonestrated in a variety of non-neoplastic hepatic disorders. The serum concentrations are more frequently increased in those disorders in which there are prominent hepatocellular necrosis and inflamation and highest values were observed in patients with viral hepatitis (Bloomer et al 1975)

The aim of our present study is to determine the serum level of A.F.P. in cases of billharzial hepatic fibrosis, and in cases with chronic active hepatitis.

REVIEW OF LITERATURE

Chapter I

Physiology of A.F.P.

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Physico-Chemical Properties :-

A.F.P. is a single poly-peptide chain glycoprotein with a molecular weight ranged from 64,000 - 70,000 and a sedimentation constant of 4.5. It contains 3-4 % carbohydrates (Ruoslahti at al, 1971, 1974) Hexose, Hexosamine and Sialic acid occur in a ratio of 2.2: 1.2 :0.9 by weight (Purves et al, 1970)

It carries physico-chemical properties very similar to albumin but human A.F.P. is slightly larger than albumin. Failure of immunological cross reactions as well as differences in their N and C terminal amino acid sequence indicate the presence of extensive structural differences between native forms of human albumin and A.F.P. The A.F.P. molecule contains high content of cysteine but with no disulphide bonding. Like albumin A.F.P. can bind oestrogen but it can not bind testosterone, though this steroid is strongly bound to albumin.(Shuster et al, 1974)

Production of A.F.P. :-

During foetal life, production and secretion of A.F.P. into the serum begins with differentiation of the foetal liver which stems from a bud from the foregut. Early in the gestation, the yolk sac and the mucosa of the gastro-intestinal tract synthesize A.F.P. but by eighteenth week the liver surpasses the yolk sac in size and becomes the major site of A.F.P. synthesis.
(Gitlin et al, 1967, 1972)

At a cellular level, most hepatocytes are initially involved in A.F.P. synthesis by the sixth week of gestation of foetal life, but as the serum level of A.F.P. commences to fall, the numbers of hepatocytes involved in its synthetic process decline and tend to be those situated around the central vein. The Kupffer cells , bile ducts, epithelial and haemopoietic cells do not appear to synthesize A.F.P. at any time. (Engethardt 1969)

Dallner and his colleagues (1966) have shown that several fine and enzymatic alternations occur in the hepatocytes immediately before and after birth. This perinatal transformation of hepatocytes from foetal to adult type is associated with rapid suppression of A.F.P.synthesis and secretion and it becomes undetectable several days to a few weeks after birth. (Abelev 1971)

The recent development of radio-immuno-assay R.I.A. techniques resulted in demonstration of small amounts of A.F.P. in the serum of healthy adults so that like carcino-embryonic antigen (C.E.A.) there does not appear to be complete gene suppression as was originally considered from data of less sensitive methods. (Abelev et a1, 1967) .

Thomas et a1,1972 postulated that the renewed production of A.F.P.by adult liver cells, may reflect the presence of a population of immature hepatocytes.

Normal Values of A.F.P. :-

A.F.P. is synthesized in early foetal life. The foetus increases its production of A.F.P. until the 20 th week. It reaches its maximum level about 12 - 15 weeks where it reaches up to the level of (2 - 4 gm/L), after which the concentration falls to around 10 - 15 mg/L at term.

By the 34 weeks of gestation A.F.P. synthesis is virtually shut off. The concentration in the newborn rapidly declines according to a calculated biological halt life time of 3 - 5 days, by two years of age, serum A.F.P. level reaches (10-20 mg/L) (Gitlin 1977)

In normal adult, trace amounts of A.F.P. may be found in the serum, values above 40 ng/ml are considered elevated. (Bloomer et al, 1974)

99.5 percent of non pregnant females had A.F.P. level below or equal 5 ng/ml During pregnancies,

there is gradual rise in the A.F.P. concentration in maternal serum but values above 15 ng/ml are not reached until the 14 or 15 weeks of gestation. The mean concentration increases up to 100 - 600 mg/L followed by decline to (40-400 mg/L) at term. (Johnsson et al., 1977)

Phisiological Function of A.F.P.

Foetal protein may have growth stimulating properties and such a role has been suggested for A.F.P. It is suggested that A.F.P. has an osmotic and transport functions similar to albumin. Rat A.F.P. was found to have high affinity to bind estradiol and estrone. It is proposed that A.F.P. may function in some specific manner in binding of estrone and estradiol during pregnancy but unfortunately studies of human A.F.P. revealed the lack of oestrogen binding properties of this molecule. (Swartz and Soloff 1974)

A.F.P. was found to have an immuno-suppressive function on antibody synthesis when administered in Vivo to murines. It was found also that it is of non cytotoxic suppressor response. T. Lymphocytes surface was found to bind A.F.P. The existence of immunosuppression protein either during gestation or during neoplasia has a definite appeal since both conditions present foreign