PLASMA FIBRONECTIN IN CHILDREN WITH POST HEPATITIC LIVER DISEASES

THESIS

Submitted for partial fulfilment of
The Master Degree in Pediatrics

BY

Maha Mohamed Mostafa Mohamed
M.B., B.Ch.

SUPERVISED BY

PROF. DR. SAADIA ABDEL FATTAH
Prof. of Pediatrics
Faculty of Medicine, Ain Shams Univ.

Assisted by

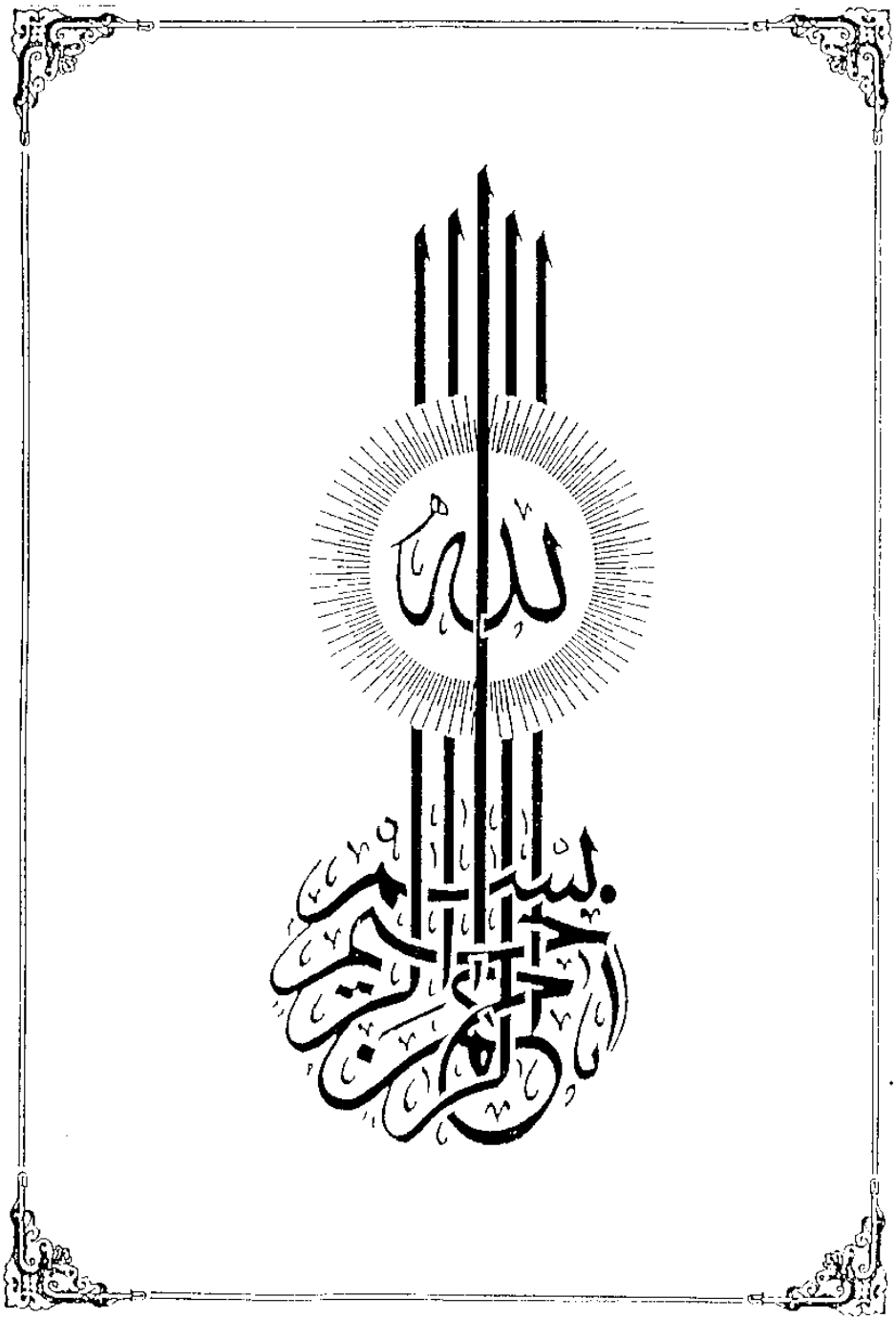
DR. FARIDA EL BAZ
Lecturer of Pediatrics
Faculty of Medicine, Ain Shams Univ.

and

DR. MAHA EL TAHAWY
Lecturer of Clinical Pathology,
Faculty of Medicine, Ain Shams Univ.

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
1989

TO MY PARENTS



ACKNOWLEDGEMENT

I would like to express my deepest gratitude to my **PROF. DR. SAADIA ABD EL FATTAH,** Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her constant encouragement, guidance and efficient, supervision and for her constructive criticism through out this work.

I wish to express my great thanks to **DR. FARIDA EL BAZ,** Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her continuous support help and supervision.

Also, I would like to express my sincere thanks to **DR. MAHA EL TAHAWY,** Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her kind help and encouragement.

I am heartly feel deeply indebted to **DR. SHERIN ABD EL FATTAH,** Assistant Prof. of Pediatrics,Faculty of Medicine, Ain Shams University, for her great support and valuable guidance,in revising this thesis in Hepatology Clinic.

Finally, I would like to express my thanks appreciation and gratitude to all my senior staff and Colleagues of Pediatrics Department and our patients whom without their help , this work would not be finished.

***

C O N T E N T S

***

LIST OF ABBREVIATION

- Fibronectin = FN
- Respiratory distress syndrome (RDS)
- Disseminated intravascular coagulopathy (DIC).
- Hepatitis B virus = HBV
- Hepatitis A virus = HAV.
- Hepatitis B surface antigen = HB_sAg
- Hepatitis B core antigen = HB_cAg
- Hepatitis B_e antigen = HB_eAg
- Chronic active hepatitis = C A H
- Chronic persistant hepatitis = CPH
- Hepato cellular carcinoma = HCC
- Hepatitis delta virus = HDV.

***

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

Fibronectin is recently considered to be one of the most important members of the immune system. Fibronectin has an important role in a variety of functions including cell adherence, spreading, tissue differentiation as well as opsonization of particulates (Bohnsak, et al.1986). The liver is involved in the turn over of fibronectin in two different ways i.e. hepatic synthesis which contributes to plasma fibronectin pool and also in other way removal of fibronectin opsonized material from the circulation by kupffer cells (Hofeler and Kingemann,1984).

Liver diseases affect the fibronectin levels in blood, in acute hepatitis significant elevation of plasma fibronectin occurred (Mastuda et al.,1982).

However decreased in plasma fibronectin levels has been shown in chronic liver diseases. A correlation between decreased its plasma levels and severity of inflammatory and necrotic changes was found. It was suggested that the level of plasma fibronectin may reflect the severity of tissue injury resulting from liver diseases (Jitoku, et al., 1986). It was found also that a lower plasma level of fibronectin have been obtained in patients with portal hypertension than cirrhotic patients without evidence of portal hypertension (Foster et al., 1983).

So, **The Aim of this study** is to determine the changes in the level of plasma fibronectin in children with acute viral hepatitis and with chronic hepatitis and to correlate its level with different liver function tests.

***

REVIEW OF LITERATURE

FIBRONECTIN

Definition :

The term fibronectin describes a family of structurally and immunologically related high molecular weight glycoprotein that are present on many cell surfaces, in extracellular fluids, and in connective tissues (Mosesson and Amrain, 1980). Fibronectin is a glycoprotein with a molecular weight of 440,000 and is composed of two mainly identical subunits, held together with disulphide bonds (Mosher and William, 1978), (Stathakis et al., 1981) - (Scholmerich et al., 1984).

Fibronectin (FN) is existing in an insoluble form on cell surface and in a soluble form in the plasma (Scholmerich et al., 1984 - Jaishree et al., 1985).

The word "Fibronectin" itself was created to emphasize the propensity of the protein to bind to fibrous protein like collagen and fibrin (fibre, fiber and nectare to bind (Mosesson, and Amrani, 1980).

Historical Events : (1948-1975)

Morrison et al., (1948) described a protein component of fibrinogen containing fractions that was cold insoluble and, unlike fibrinogen was not thrombin coagulable, displayed a more rapid anodal electrophoretic migration rates and higher sedimentation coefficient than did fibrinogen, Later, physicochemical analysis reported in 1955 by Edsall

et al, lead to suggestion that cold insoluble globulin was a modified dimer of fibrinogen. Shortly there after, Smith and Vankorff in 1957, described a protein with properties similar to those of cold - insoluble globulin that they had found in a heparin - induced cold precipitate of either normal or pathologic plasma . subsequent clasification of these observation began by Mosesson et al., (1968), with investigation of a patient presenting with a chronic intravascular coagulation syndrome secondary to an occult neoplasm the illness was characterized by the persistance of a pathologic cold induced plasma precipitate termed "cryofibrinogen". The soluble cryofibrinogen was particularly coagulable by thrombin, thus providing that fibrinogen was present as another major component resembling cold-insoluble globulin was also found in fractions and was shown to be immunochemically identical with a normal serum protein unrelated to fibrinogen.

In early 1970 a number of investigations had focused on the changes that occurred in all surface proteins of fibroblasts as a consequence of transformation by oncogenic viruses.

Particular attention was paid to a large transformation, sensitive glycoprotein of high molecular weight, that was released from the fibroblast cell surface into the culture media (Hynes and Bye, 1974; Roushahti

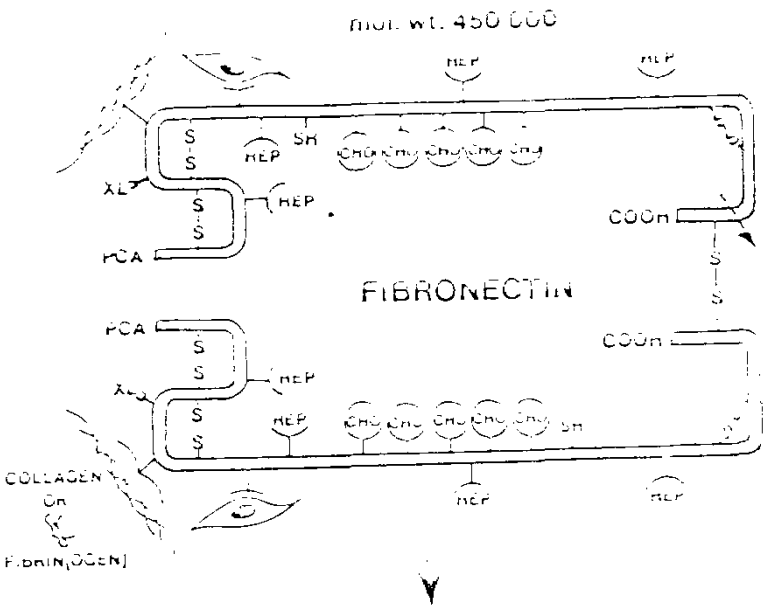
and Vaheri 1974; Blumberg and Robbins 1975; Ruoshahti et al., 1975). The report by Ruoslahti and Vaheri in 1975 that cold - insoluble globulin was antigenically identical to large transformation - sensitive glycoprotein, brought to light the uniqueness of fibronectin as both a cell surface, matrix protein and a blood protein and has stimulated numerous investigations on all forms of this protein.

...

FIBRONECTIN STRUCTURE

Structural studies of FN derived from cell surfaces, tissue culture medium, or extracellular fluids have been complicated by the presence of molecular heterogenity (Juffe and Mosher, 1978). Despite this, a fairly detailed outline of the basic molecular architecture can be sketched (Fig.1). Since there are many similarities and only a few significant differences among the various fibronectins. Most circulating FN molecules have a molecular weight of 480,000 and are composed of two disulfide - bridged chains of approximately equal size (Mosesson et al., 1975), these bridges are located very close to one end of the molecule, probably at the COOH-terminus (Yamada et al., 1978) disulfide bridging may be required for binding of FN to gelatin and to cells (Balian et al., 1979).

Intrachain disulfide bridges are clustered in the terminal third of each chain, most of them being at the NH2-terminal end. Jilek and Hormann (1977) have identified a disulfide containing plasmic fragment of molecular weight 27,000 containing a label introduced by factor XIIIa Mosher et al., 1980 have also reported on factor XIIIa reactive tryptic fragment of similar size that contains the site(s) involved in crosslinking to collagen. The cross linking site is distinct from the site responsible for tight binding with collagen, both the binding and cross linking regions are contained in a 70,000 molecular weight fragment generated in thrombin digests that have



Structural Model of Plasma Fibronectin

Mosesson and Amrani (1980)