Ain Shams University

Faculty of Medicine

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PLASMA FIBRONECTIN IN PRE-ECLAMPSIA

Thesis

Submitted For Partial Fulfilment Of Master Degree In

Gynaecology And Obstetrics

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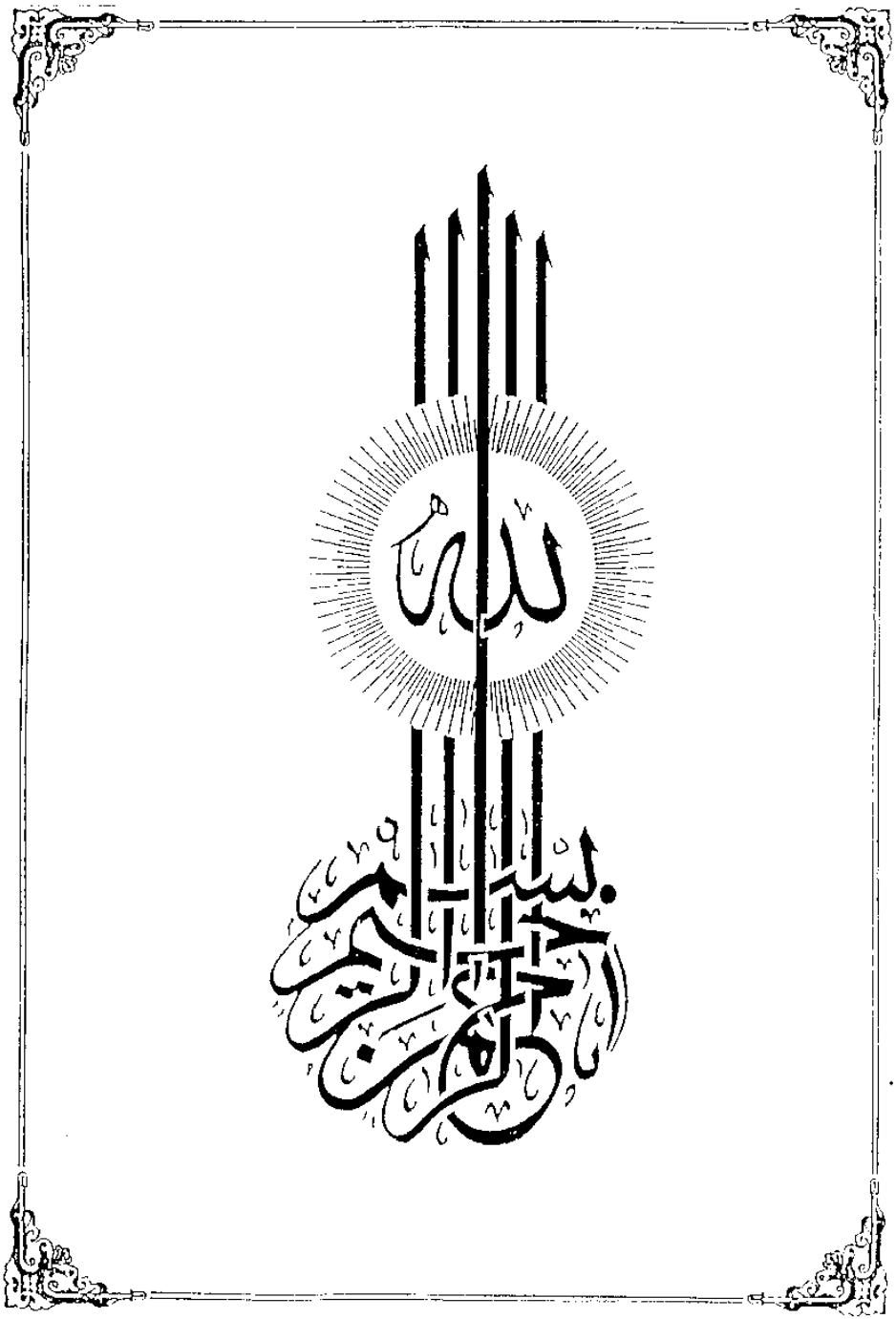
بسم الله الرحمن الرحيم

" قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العليم الحكيم "

صدق الله العظيم

سورة البقرة (٣٢)



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CONTENTS

INTRODUCTION

INTRODUCTION

Fibronectin is a high molecular weight glycoprotein which has a soluble plasma form and an insoluble tissue form. it plays a wide role in hemostasis and tissue repair at sites of vascular injury ***(Mosher, 1980)***. Levels of normal circulating fibronectin (200 - 400 ug / ml).

It is linked to the function of the coagulation system and platelets, and is intimately related to the vascular endothelial basement membrane. Plasma fibronectin participates in the clearing of different particles, fibrin and fibrin degradation products from blood ***(Eriksen et al., 1987).***

Plasma fibronectin level increases in normal pregnancy (**Eriksen et al.,1987)** in contrary to the view held by **(Ganrot 1972)**. It is elevated in patients with connective tissue disease ***(Bruhn and Heimberger, 1976)*** and decreased in several disease processes including malignancies, disseminated intravascular coagulation ***(Mosher and Williams, 1978)*** as well as after trauma or operation ***(Stubbs et al., 1984).***

Generalized arteriolar spasm with secondary interruption of blood flow and haemorrhage in the microcirculation suspected to have a patho-physiologic role in pre-eclampsia and may be the initiating mechanism of the characteristic renal lesions ***(Pritchard et al , 1985).***

The increased plasma fibronectin concentrations seen in pre-eclampsia could be explained by either vascular endothelial damage with direct release of converted tissue fibronectin into the blood stream or by increased synthesis of fibronectin by the vascular endothelium ***(Stubbs et al., 1984).***

EriKsen et al., (1987) suggested that plasma fibronectin level is increased in pre-eclamptic patients and that its level serves as an early indicator of endothelial cell damage.

AIM OF WORK :

The aim of this work is to measure plasma fibronectin in pre-eclamptic patients and to correlate its level with the severity of the disease and the fetal outcome.

REVIEW

OF

LITERATURE

A. FIBRONECTIN

FIBRONECTIN

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(A) DEFINITION AND NOMENCLATURE :

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* The term fibronectin describes a family of structurally and immunologically related high molecular weight glycoproteins, that are present on many cell surfaces, in extracellular fluids, in connective tissue and in most basement membranes ***(Mosesson et al., 1980) (Cosio & Bakaletz 1986, Hynes 1986).***

* The name is derived from Latin origin , Fibra means fiber and nectere means to bind or to contact. ***(Kuscla et al., 1976, Mosesson and Amrani 1980, Saba et al., 1986, Hynes 1986).***

* Prior to the suggestion of the name fibronectin, the protein in its various forms has been designated by avariety of terms including :

- Large external transformation sensitive protein (LETS) **(Rouslahti et al., 1978).**
- Cell surface protein (CSP) ***(Yamada and Wentson 1974)***
- Cell adhesion factor (CAF) ***(Pearlstein 1976)***
- Galacto protein a ***(Gahamberg et al., 1974)***
- Galacto protein z ***(Blumberg and Robbins 1975)***
- Cold insoluble globulin (C I G) ***(Chen and Moseson* 1976 *)***
- Opsonic protein **(Saba, 1970)** .
- Cell spreading factor **(Grinell 1976).**
- Antigelatin factor **(Wolff et al, 1987).**

(B) PHYSIOLOGY AND BIOCHEMISTRY :

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I- Cellular Origin of Fibronectin :

- Fibronectin was first identified in fibroblast ***(Rouslahti and Damus, 1973)*** but cellular origin of fibronectin is not limited to fibroblast. Several types of epithelial cells have been found to produce fibronectin at least in vitro. These include : epithelial cells from the liver ***(Clemmensen 1984),*** Kidney ***(Chen et al, 1977)***, breast ***(Smith et al., 1979)*** and amniotic membranes ***(Crouch et al, 1978)***. Other cell types that produce fibronectin include myoblast ***(Hynes. 1973)***, macrophages ***(Alitalo et al., 1980)*** and endothelial cells ***(Mosher, 1978)***. Endothelial cells and liver cells may be the source of circulating *fibronectin* ***(Rouslahti et al, 1981)*** Platelets may also contribute to plasma fibronectin ***(Zucker et al., 1979).***

  * Interacellular fibronectin exists in structures concerned with protein synthesis and secretion, namely in the rough endoplasmic reticulum and Golgi apparatus : ***(Yamada et al., 1980)*** .

II . Distribution of Fibronectin :

The distribution of fibronectin is wide spread. A striking characteristic feature of fibronectin is its existence both as an insoluble connective tissue protein and soluble plasma protein. Cellular culture similarly contain insoluble fibronectin in the cell layer and soluble fibronectin in the different compartments,

1. Intracellular 2- At the cell surface and 3- In the extracellular matrix ***(Hedman et al., 1978)***. Fibronectin was also found to be abundant in many developing tissues but oftenly absent from their corresponding mature tissue ***(Wartrovaara et al., 1974)***.

* During embryogenesis fibronectin is first detected on cells of blastula inner cell mass. At later developmental phases, fibronectin is lost or becomes redistributed concomitantly with differentiation of mesenchymal cells into muscles, cartilage and renal tubular epithelium. ***(Wartiovaara et al., 1976).***

- In tissue culture, fibronectin usually appears as fibrillar matrices that are situated on cells, between cells and substratum ***(Vaheri and Mosher 1978 , Yamada and olden, 1978)*** This pattern is consistent with the role of fibronectin in the spread and adhesion that take place among cells and the substratum. ***(Pearlstein 1976 , Grinnel 1978).***

Stenmann and Vaheri (1978) Using immunofluorescence localization technique had demonstrated that all the blood vessels including capillaries contained a zone of fibronectin corresponding to the basement membrane of the endothelium, the internal elastic lamina which contains elastic fibres, was outside this zone and clearly separated from it. Fibronectin was also present in the loose connective tissue of the adventitia. In muscular arteries, fibronectin was further found around the smooth muscle cells of the media. In non muscular arteries, the media contained these strands of fibronectin.

It is not clear weather the fibronectin of the basement membranes is produced by connective tissue cells or by adjacent epithelial cells. Data from in vitro experiments support both possibilities ***(Rouslahti et al., 1978) (Wartiovaara et al., 1976).***

III- Biochemical structure :

Structural studies of fibronectin derived from cell surfaces, tissue culture medium, or extracellular fluids have been complicated by the presence of molecular heterogenity. ***(Mosesson et al., 1975 , Yamada et al., 1977).***

In spite of this, a fairly detailed out line of the basic molecular architecture can be out lined as (Figure 1) ***(Mosesson and Amrani, 1980).***

There are many similarities and only a few significant differences among the various fibronectin.

Most circulating fibronectin molecules have amolecular weight of 450,000 daltons (one dalton is the mass of a hydrogen atom).

Each molecule is a dimer consisting of two or more or less identical subunits (polypeptide chains) linked by disulphide bridges **(Mosesson et al., 1975, Mosher 1975, Hynes 1986).**

These bridges are loacated very close to one end of the molecule, probably at the COOH-terminus **(Hynes et al., 1978; Wagner and Hynes, 1979).** Intrachain disulphide bridges are clustered in the terminal thirds of each subunit, most of them being at the NH_2 - terminal end. **(Fukuda and Hakomori, 1979).** There also appears to be a significant number of free sulfhydryl groups in plasma fibronectin molecules, amounting to 1 or 2 per dimeric molecule **(Pearlstein and Gold 1980)**

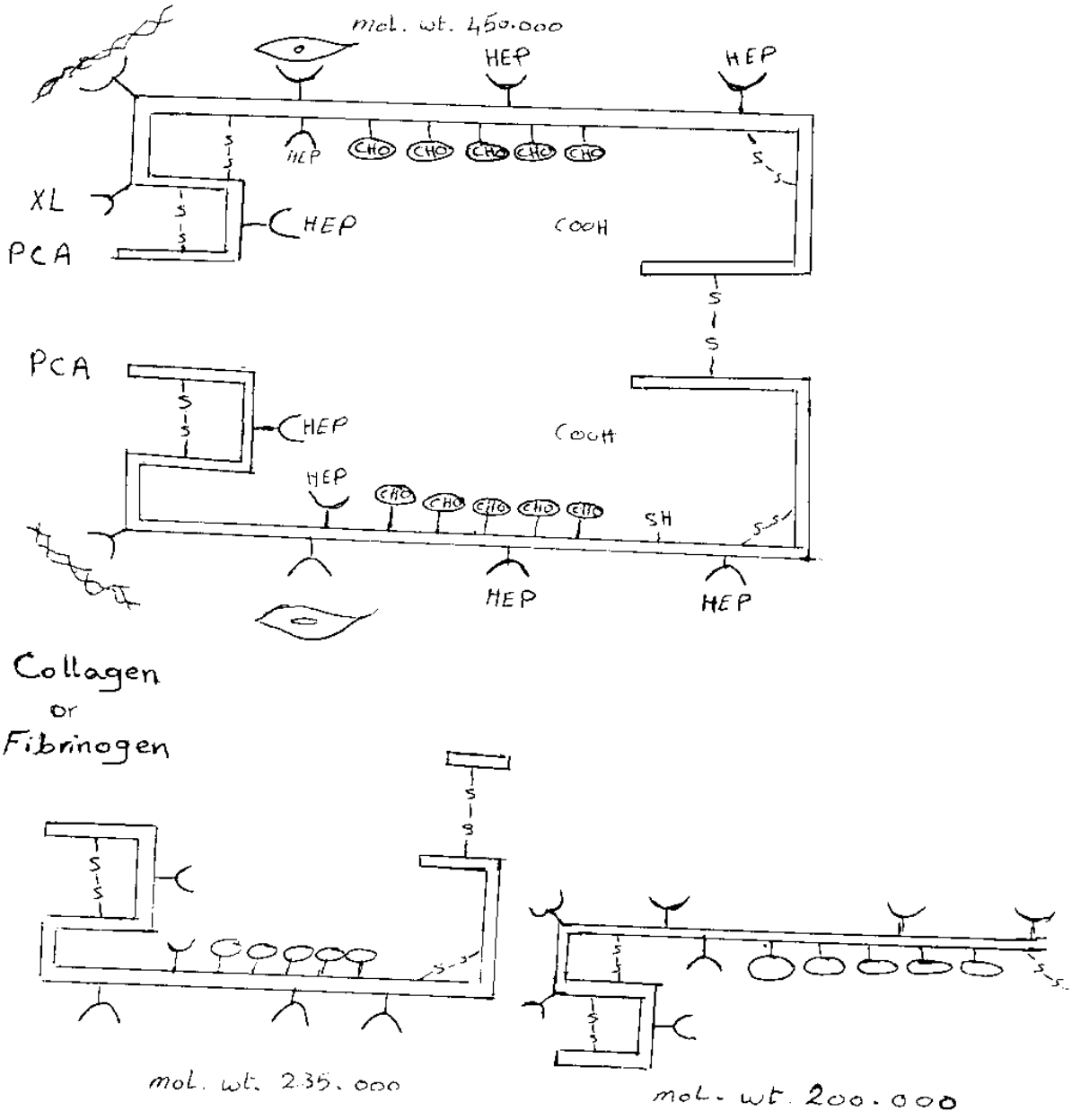

Fig (1) : Structural model of plasma fibronectin

Most circulating molecules are composed of 2 or more or less identical chains of approximate mol. wt. 220,000, each linked near the COOH terminal end by desulphide bridging (s.s). The NH2 terminus is designated PCA (pyrrolidone carboxylic acid). The dashed arrow indicates orgion in the dimeric molecule which is cleaved during the course of hydrolysis by several proteolytic enzymes. Form Mosesson M. W. and Amrani D. L. the structure and biologic activities of plasma fibronectin. **(Blood, 56, 2,145, 1980)** .