# Plasma Fibronectin, Lipid Profile and Transaminases in Diabetics with Fatty Liver

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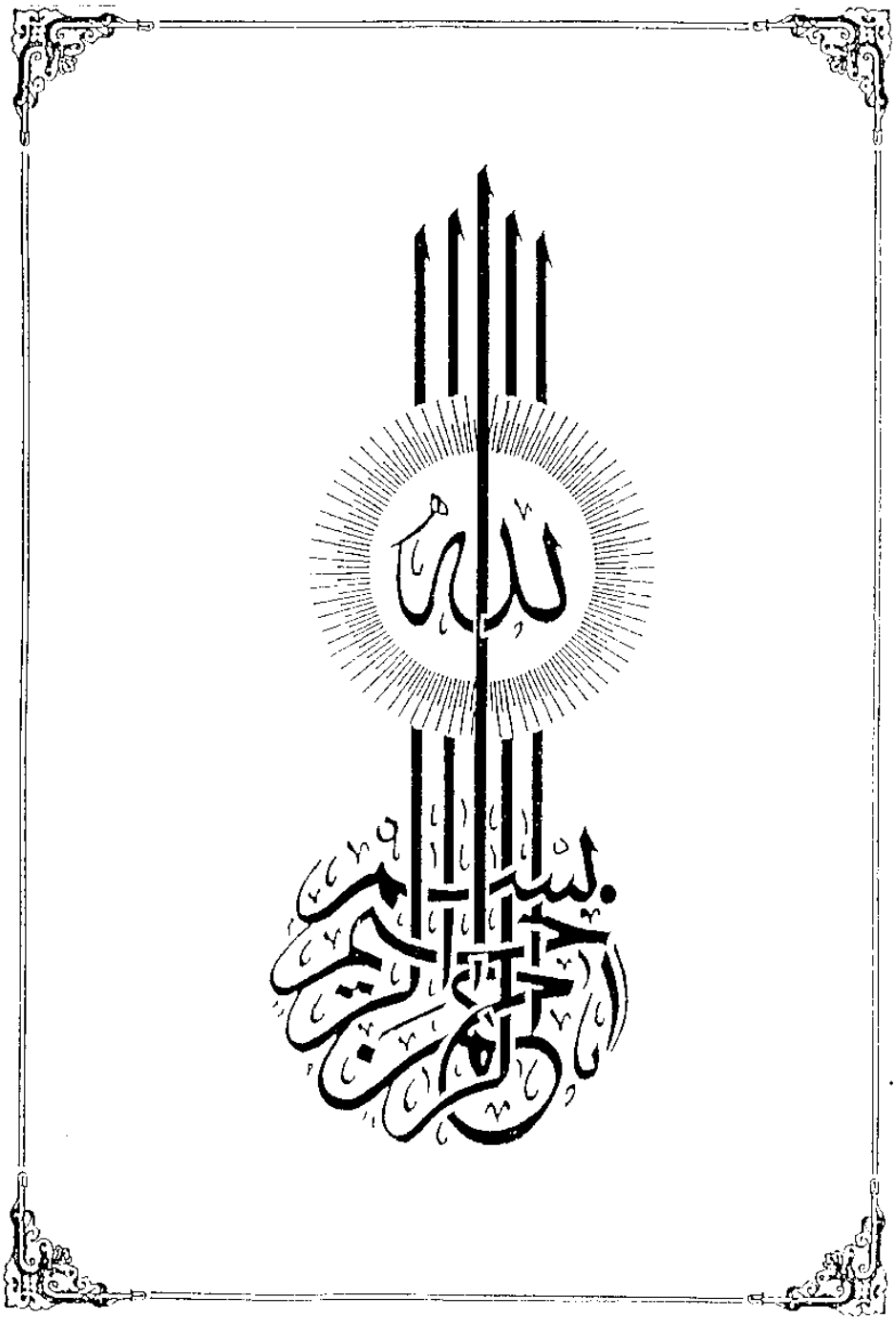

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## Introduction:

Fatty liver usually reflects excess accumulation of triglycerides. It usually reflects an imbalance between the rate of triglyceride biosynthesis and secretion into the plasma (**Iwamuro, 1989**).

Conditions associated with fatty liver include: Obesity, protein-calorie malnutrition, diabetes mellitus, corticosteroid; ethanol and other drugs, Reye's syndrome and acute fatty liver of pregnancy.

In diabetics, type I- the insulin dependent, most cases with fatty liver are associated with prolonged acidosis and the enlargement is due to excess glycogen deposition.

On the other hand, type II- the non-insulin dependent, the hepatic enlargement is due to fatty infiltration in addition to excess glycogen deposition and most of the patients are obese.

Fatty liver has been associated in many instances with hypercholesterolemia and hypertriglyceridemia. More recently increased level of plasma fibronectin has been associated with different complications of diabetes, particularly those associated with micro-and macrovascular lesions **(Borrego et al., 1991)**.

## Aim of the work:

The aim of this work is study the plasma fibronectin concentrations, lipid profile and transaminases in diabetics with fatty liver in attempt to answer whether diabetes without obesity has a role in the pathogenesis of fatty liver and to evaluate a possible diagnostic and prognostic value of these parameters in such patients.

# List of Abbreviations

| | |
|---|---|
| **AFLP** | Acute fatty liver of pregnancy. |
| **AIDS** | Acquired immunodeficiency syndrome. |
| **ALK. Ph.** | Alkaline phosphatase. |
| **ATP-ase** | Adenosine triphosphatase. |
| **CT** | Computed tomography. |
| **DCCT** | Diabetes Control Complications Trial. |
| **DM** | Diabetes mellitus. |
| **EDTA** | Ethylene diamine tetra-acetic acid. |
| **EGF** | Epidermal growth factor. |
| **FBS** | Fasting blood sugar. |
| **Fig.** | Figure. |
| **GGT** | Gama glutamyl transferase. |
| **HDL** | High density lipoprotein. |
| **HS** | High significance. |
| **IDDM** | Insulin dependent diabetes mellitus. |
| **LDL** | Low density lipoprotein. |
| **MCP-1** | Monocyte chemotactic protein-1. |
| **M-CSF** | Macrophage - colony stimulating factor. |
| **MRI** | Magnetic resonance imaging. |
| **NIDDM** | Non-insulin dependent diabetes mellitus. |
| **NS** | Non significance. |
| **OGGT** | Oral glucose tolerance test. |
| **OX-LDL** | Oxidized low density lipoprotein. |
| **PP** | 2-hours postprandial blood sugar. |
| **S** | Significance. |

| | |
|---|---|
| **SD** | Standard deviation. |
| **SGOT** | Serum glutamate oxaloacetate transaminase. |
| **SGPT** | Serum glutamate pyruvate transaminase. |
| **TGF-B** | Transforming growth factor-B. |
| **TNF** | Tissue necrosis factor. |
| **USA** | United States of America. |
| **VLDL** | Very low density lipoprotein. |
| **WHO** | World Health Organziation. |

# REVIEW OF LITERATURE

# FIBRONECTIN

## Introduction:

The term fibronectin describes a family of structurally and immunologically related high molecular weight glycoproteins **(Amrani et al., 1985)** present on the surface of cells, in extracellular fluids, in plasma and in basement membranes **(DiGirolamo et al., 1993)**. Fibronectin exists in two predominant forms: soluble in plasma and insoluble fibrillar in the extracellular matrices (cell surface) **(Somers and Mosher, 1993)**.

Prior to the suggestion of the name fibronectin, it was designated by a variety of terms, which were named according to sources or biological activity, that later proved to be nearly identical and were all named fibronectin **(Yamada and Olden, 1978)**.

At present, there is a general acceptation of the term fibronectin, which comes from latin roots "Fibra" meaning fiber and "necrete" meaning to bind , link or connect **(Mosher, 1980)**.

## Synthesis and breakdown:

Fibronectin is synthesized by a wide variety of cells; fibroblasts, platelets, amniotic cells, endothelial cells, macrophages, liver epithelial cells, smooth muscle cells, mast cells, marrow adherent cells, prostatic cells, kidney mesangium and basement membrane **(Herris et al., 1988)**.

The plasma fibronectin is mainly synthesized and secreted by hepatocytes; in addition, macrophages and endothelial cells share in its production to a lesser extent **(Hynes, 1990)**, which evidence suggests that most, if not all, circulating fibronectin is produced by hepatocytes **(Gonzalez - Calvin et al., 1982)**. The relationship between plasma fibronectin and cell surface "tissue" fibronectin has not been well established and it seems likely that a dynamic equilibrium exists between them **(Mosher, 1984)**.

Fibronectin is sensitive to neutral tissue proteinases. Destruction may be involved after mast cell activation and in inflammatory conditions in vivo **(Alan et al., 1981)**.

## Structure:

Structural studies of fibronectin derived from cell surfaces , tissue culture medium, or extracellular fluids show molecular heterogenecity **(Mosesson and Amrani, 1980)**. All fibronectins are composed of 200,000-240,000 molecular weight subunits **(DiGirolamo et al., 1993)**. They are hetero- or homodimeric cell adhesive glycoproteins **(Wu et al., 1993)**, as plasma fibronectin is a dimmer of subunits; and cell surface fibronectin, a multimer of very similar subunits to those of plasma fibronectin, which are disulfide-bounded **(Jones et al., 1986 and Kasbaoui et al., 1989)**. The inter-chain disulfide bridges are located close to the C-terminus of the molecule **(Wagner and Hynes, 1980)**.

Each subunit has interchain disulfide bonds, which are grouped in the terminal third of each chain, most of them present at the $NH_2$-terminus and some are also present at the C-terminus **(Furie and Rifkin, 1980). (Fig.1,2).**

Fibronectin contains distinct binding domains for a variety of substrates such as fibrin, collagen and proteoglycans and functions in cell-to-cell and cell-to-matrix adhesion as well as in the organization of extracellular matrices **(Grinnell, 1984). (Fig. 3).**

There is a qualitative difference in the carbohydrate part of different fibronectins. Both plasma and cell surface forms have similar amounts of carbohydrate, about 5%, but difference in the sugars have been present **(Mosesson and Amrani, 1980)**. The major sugars in plasma fibronectin molecule are mannose,galactose, N-acetyl glucosamine and sialic acid. The cell surface form contains more fucose and much less terminal sialic acid **(Fukuda and Hakomori, 1979)**.

On the other hand, several minor fibronectin components of smaller size than the two chain structure have been identified in plasma molecules and most of them range in molecular weight from 146,000 to 235,000 daltons. They may be derived by catabolic processes and some of them may reflect cleavage near the $NH_2$-terminus of a parent chain **(Mosesson and Amrani, 1980)**.