Lipoprotein Abnormalities Accompanying Diabetic Nephropathy

A Thesis
Submitted in Partial Fulfillment of Master Degree in Internal Medicine

By
Physician: Pierre Samir Mosaad
MB; BCh.

Under Supervision of

Prof. Dr. Hala Ali Gamal El Din
Professor of Internal Medicine
Faculty of Medicine - Cairo University

Prof. Dr. Ossama Khalaf Allah
Professor of Clinical Pathology
Faculty of Medicine
Cairo University

Prof. Dr. Hala El Mofty
Professor of Ophthalmology
Faculty of Medicine
Cairo University

Faculty of Medicine
Cairo University
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ABSTRACT

- **Background:**

There is now much evidence that dyslipidemia can favor progression of renal damage in both **diabetic and nondiabetic diseases.** Out of all tested lipid parameters **only plasma apo B concentration remained significant as a predictive factor of progressive renal failure**.

- **Objectives:**

To prove that apolipoprotein B -100 can be used as an early detected risk factor to assess diabetic nephropathy and retinopathy.

- **Methods:**

We randomly selected 56 patients of both Type 1 and Type 2 diabetes mellitus. We proved that they have diabetic nephropathy through elevated albumin to creatinine ratio. Fundus examination and flourescein angiography were done to detect retinopathy grade.

- **Conclusion**

Apolipoprotein B levels usually increase with the rise of degrees of nephropathy and retinopathy.

- **Keywords:**

Apolipoprotien B, Diabetic nephropathy, Diabetic retinopathy.

To my mother and my father

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A/C	Albumin /Creatinine ratio
ACE	Angiotensin-converting enzyme
ACEi	Angiotensin-converting enzyme inhibitor
AER	Albumin excretion rate
AGE	Advanced glycation endproduct
Apo B	Apolipoprotein B
AR	Aldose reductase
ARB	Angiotensin receptor blocker
AT_1	Angiotensin II type 1 receptor
CKD	Chronic kidney disease
Cr	Creatinine
CSME	Clinical significant macular oedema
CVD	Cardiovascular disease
CHF	Congestive heart failure
CABG	Coronary artery bypass graft
DCCT	Diabetes Control and Complications Trial
DD	Disc diameter
DME	Diabetic macular edema
DR	Diabetic retinopathy
E GFR	Estimated glomerular filtration rate
ER	Endoplasmic reticulum
ETDRS	Early Treatment Diabetic Retinopathy Study
GFR	Glomerular filtration rate
IRMAs	Intraretinal microvascular abnormalities
LDL	Low density lipoproteins
MDRD	Modification of Diet in Renal Disease
MI	Myocardial infarction
NO	Nitric oxide
NPDR	Non-proliferative diabetic retinopathy
NSC	National Screening Committee
NVD	New vessel at disc
NVE	New vessels elsewhere
PDGF	Platelet-derived growth factor

PDR	Proliferative diabetic retinopathy
PKC	Protein kinase C
PTCA	Percutaneus transluminal coronary angiography
RAS	Renin-angiotensin system
ROS	Reactive oxygen species
UAE	Urinary albumin excretion
UKPDS	United Kingdom Prospective Diabetes Study
UTI	Urinary tract infection
VA	Visual acuity
VLDL	Very low density lipoproteins
VEGF	Vascular endothelial growth factor
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy

INTRODUCTION

There is now evidence that dyslipidaemia can favor progression of renal damage in both diabetic and nondiabetic diseases.

Microalbuminuria is often found in association with hyperlipidemia, especially in patients with diabetes and hypertention.

Urinary protein loss may increase serum lipoprotein levels. Alternatively, hyperlipidemia may contribute to the progression of chronic kidney disease by a mechanism similar to atherogenesis.

The cornerstone of our study was **apolipoprotein B -100**. It is found in VLDL, IDL or LDL and synthesized by the human liver.

Apolipoprotein B (apo B) is the structural protein of all proatherogenic lipoproteins, so it could provide the best estimate of the total number of atherogenic particles. Some studies showed that plasma apo B concentration is a significant predictive factor of progressive renal failure. All apolipoproteins except apoB-100 are transferred to other lipoproteins. Apolipoprotien B may be the only lipoprotein to rise in normolipidemic diabetic patients. For all the previous reasons we chose apolipoprotein B for our study.

Elevated lipids may increase the morbidity of macular edema and affect the severity of diabetic retinopathy.

It is likely that patients with diabetic retinopathy are at higher risk to progress to overt nephropathy. So the eye is considered the window of kidney in both type1 and type 2 Diabetes.

AIM OF WORK

- Is to find a relation between dyslipidemia and diabetic nephropathy using apolipoprotein B-100.

- To detect patients with different grades of diabetic retinopathy and detect its relation to the degree of diabetic nephropathy.

- To find a relation between apolipoprotein B and diabetic retinopathy.

- To try to prove that apolipoprotein B -100 can be used as an early detected risk factor to assess diabetic nephropathy and retinopathy.

Diabetes Mellitus

DEFINITION AND DESCRIPTION OF DIABETES MELLITUS

Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both[1].

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia [2].

Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with **ketoacidosis** or the **nonketotic hyperosmolar** syndrome [2].

Long-term complications of diabetes include **retinopathy** with potential loss of vision; **nephropathy** leading to renal failure; **peripheral neuropathy** with risk of foot ulcers, amputations, and Charcot joints; and **autonomic neuropathy** causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of **atherosclerotic cardiovascular, peripheral arterial and cerebrovascular** disease. Hypertension and abnormalities of **lipoprotein** metabolism are often found in people with diabetes [2].

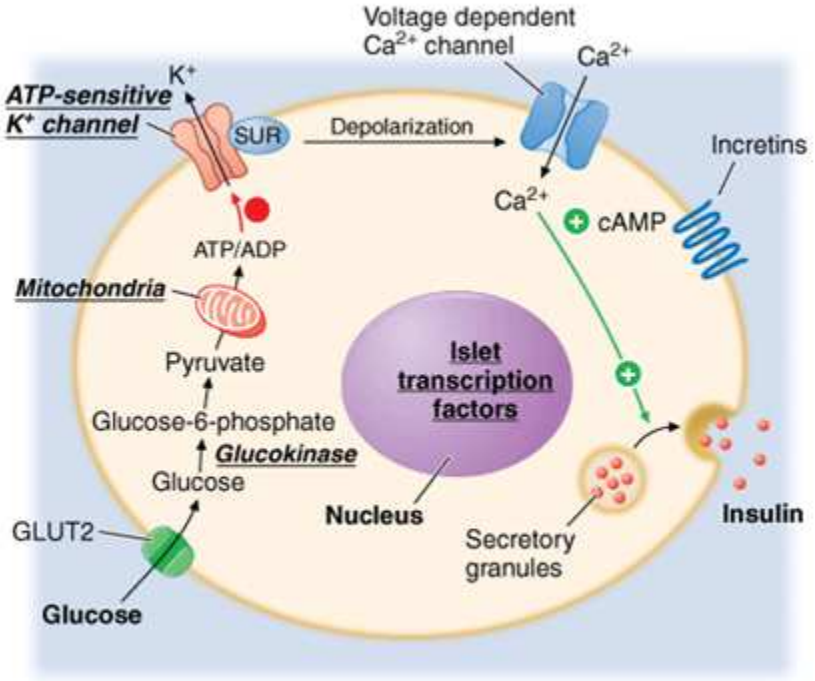

Fig 1: Mechanism of insulin secretion by beta cells.[3]

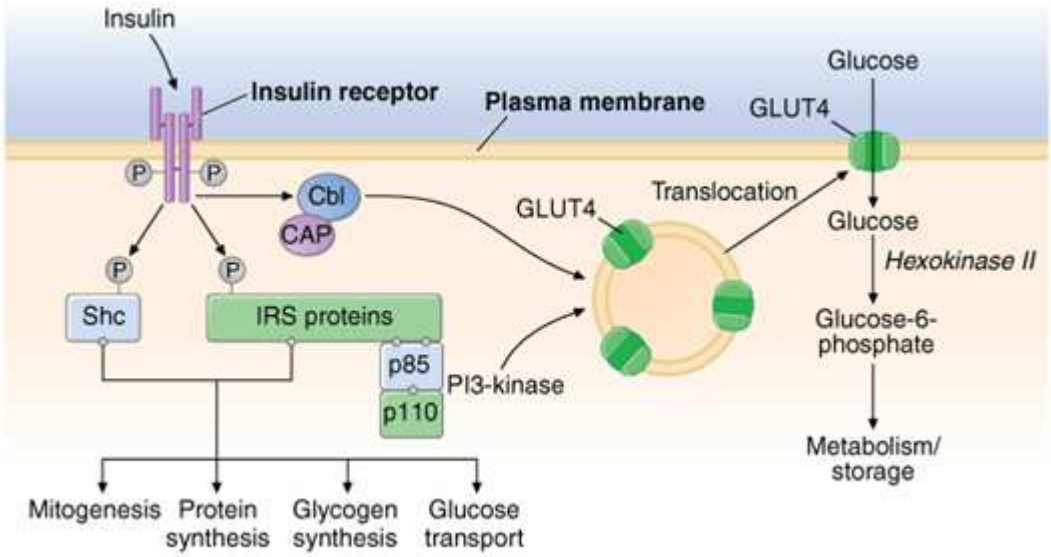

Fig 2: Mechanism of insulin action on peripheral cells.[3]

CLASSIFICATION OF DIABETES MELLITUS

Table 1: Etiological classification of diabetes mellitus [2]

ETIOLOGIC CLASSIFICATION OF DIABETES MELLITUS
I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency) A. Immune mediated B. Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III. Other specific types **A. Genetic defects of β-cell function** **B. Genetic defects in insulin action** **C. Diseases of the exocrine pancreas** **D. Endocrinopathies** e.g. Cushing syndrome and hyperthyroidism **E. Drug- or chemical-induced** e.g. Glucocorticoids **F. Infections** e.g. mumps and EBV **G. Anti–insulin receptor antibodies** **H. Other genetic syndromes sometimes associated with diabetes** e.g. Down's syndrome
IV. Gestational diabetes mellitus (GDM)

DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

The criteria for the diagnosis of diabetes are shown in **table 2**[2]. Three ways to diagnose diabetes are possible, and each, must be confirmed, on a subsequent day, by any one of the three methods given in **table 2**. (The use of the hemoglobin A1C (A1C>or =6.5%) for the diagnosis of diabetes has been recently recommended) [4].

Table 2: Criteria for the diagnosis of diabetes:

1.	FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for **at least 8 h.***
	OR
2.	Symptoms of hyperglycemia and casual plasma glucose ≥**200** mg/dl (11.1 mmol/l). **Casual** is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss*.
	OR
3.	2-h plasma glucose ≥**200** mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of **75** g anhydrous glucose dissolved in water**.**

***in the absence of unequivocal hyperglycemia**