

Lipoprotein Abnormalities Accompanying Diabetic Nephropathy

A Thesis

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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 fluorescein angiography were done to detect retinopathy grade.

- **Conclusion**

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

- **Keywords:**

Apolipoprotein B, Diabetic nephropathy, Diabetic retinopathy.

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To my mother and my father

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LIST OF ABBREVIATIONS

| | |
|-----------------------|--|
| 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 |
| AT₁ | 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 |

LIST OF ABBREVIATIONS

| | |
|--------------|---|
| PDR | Proliferative diabetic retinopathy |
| PKC | Protein kinase C |
| PTCA | Percutaneous 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 hypertension.

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. Apolipoprotein 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 type 1 and type 2 Diabetes.

INTRODUCTION AND AIM OF WORK

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 both¹.

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 hyperglycemia².

Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with **ketoacidosis** or the **nonketotic hyperosmolar** syndrome².

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 diabetes².

INTRODUCTION

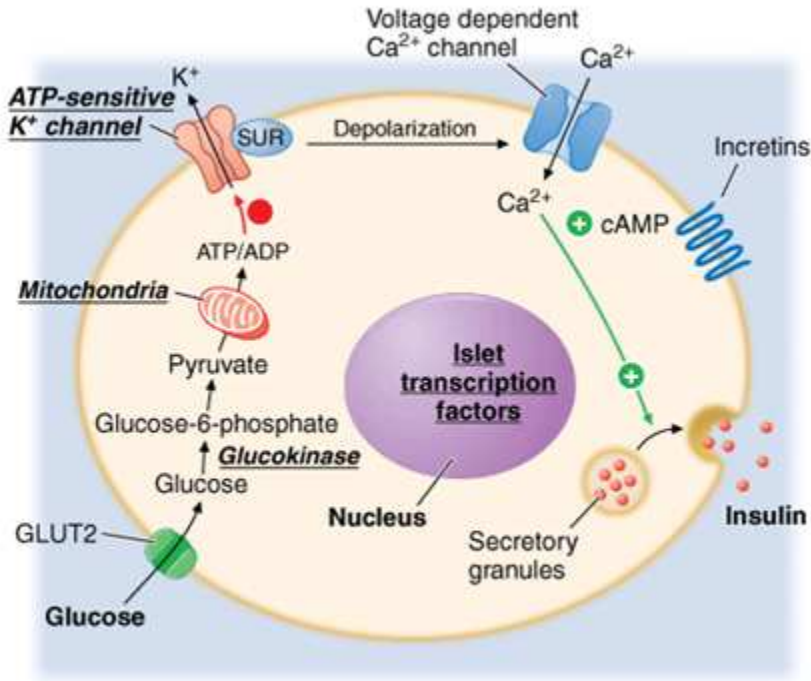


Fig 1: Mechanism of insulin secretion by beta cells.³

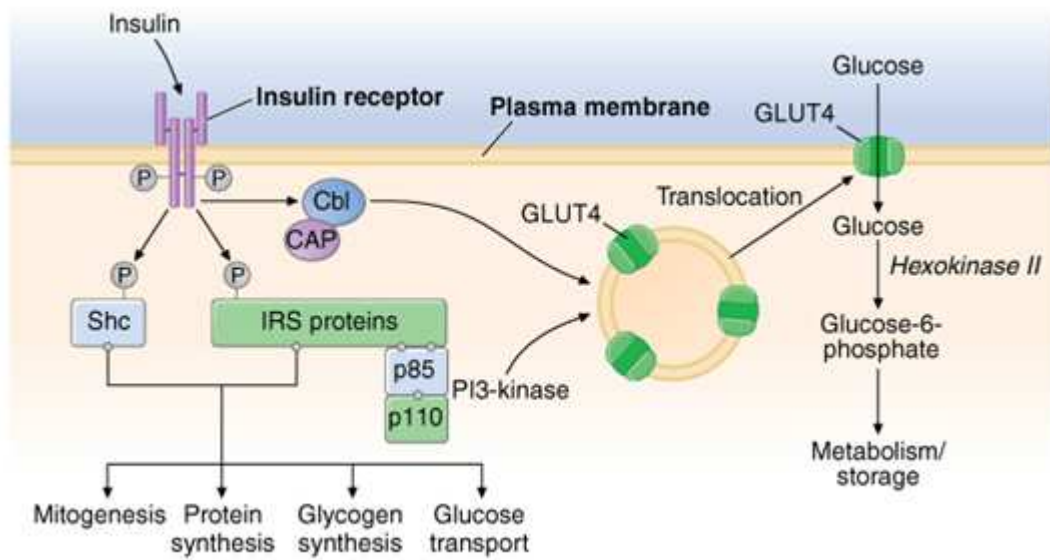


Fig 2: Mechanism of insulin action on peripheral cells.³

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)

INTRODUCTION

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 \geq 6.5%) for the diagnosis of diabetes has been recently recommended)⁴.

Table 2: Criteria for the diagnosis of diabetes:

| | |
|----|--|
| 1. | FPG \geq 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 \geq 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 \geq 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**