# Retinopathy and Dyslipidemia in Type II Diabetes Mellitus in Egyptian Patients

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## Abstract

**Purpose:** Dyslipidemia potentially contributes to microvascular disease, and this is in addition to its known effects on macrovascular disease. The aim of this study was to detect the relation between apolipoprotein B (apo B) and diabetic retinopathy (DR).

**Methods:** This is a cross sectional study conducted on 168 patients with types II diabetes mellitus. The primary outcome measures were to assess the grade of diabetic retinopathy and serum level of apo B. The Secondary outcome measures were to assess the patients' best corrected visual acuity.

**Results:** There was a significant increase in apo B in subjects with retinopathy as compared to those without retinopathy $(p<0.001)$. Correlating apo B levels to the grade of retinopathy was statistically significant $(r=0.432; p<0.001)$. Also a statistically significant relation was found between apo B and diabetic maculopathy $(p=0.003)$.

**Conclusion:** There was a statistically significant increase in apo B in subjects with retinopathy as compared to those without retinopathy, and a fair correlation between apo B levels and grade of DR. Furthermore a statistically significant relation was found between the apo B level and the presence of maculopathy.

## Introduction

Retinopathy is the most common microvascular complication of diabetes, resulting in blindness for over 10,000 people with diabetes per year. There is evidence that retinopathy begins to develop (in some patients) at least 7 years before the clinical diagnosis of type II diabetes [1]. There may be genetic components to complications; 43% of the Diabetes Control and Complication Trial (DCCT) patients in the worst glycosylated hemoglobin (A1C) quintile did not develop retinopathy, whereas 10% of those in the best quintile did develop retinopathy [2].

The prevalence of microalbuminuria among diabetic patients is 15 to 20 %. Persistence of microalbuminuria in diabetic patients is a risk marker for severe ocular morbidity [3]. Kidney microangiopathy is thought to come before retinal microangiopathy. Microalbuminuria could be a risk marker of proliferating retinopathy [4].

The control of blood lipids is one of the cornerstones in the treatment of diabetes. Apart from effects on macrovascular outcomes [5], dyslipidemia potentially contributes to microvascular disease [6]. Out of all the tested lipid parameters only plasma apolipoprotein B (apo B) concentration remained significant as a predictive factor of progressive renal failure [7].

The aim of our study was to determine the relation between apo B and diabetic retinopathy.

## Materials and Methods

Approval for the study was obtained from the hospital's ethical committee (according to the WMA Declaration of Helsinki). All patients received a thorough explanation of the study design and aims, and were provided with written informed consent.

This is a cross sectional study conducted on 168 patients with Type II diabetes mellitus usually after 5 years of diagnosis. Patients were selected from Kasr Al-Aini Cairo University Hospitals outpatient clinics of Ophthalmology and Diabetes outpatient clinics. Kasr Al-Aini hospital is a central university hospital in Cairo and is the centre for referral from most of the governorates in Egypt.

Exclusion criteria were patients with previous panretinal photocoagulation, patients taking fibrates or those already using other lipid lowering drug or were taking a lipid lowering agent during the previous 6 weeks, patients with hypothyroidism, familial hyperlipidemia, familial hypercholesterolemia, and alcoholics, to avoid false increase in apolipoproteins.

## Methods

All patients included in this study were subjected to the following:

**Ophthalmological examination:** Full ophthalmological examination was done in the form of; best corrected visual acuity (BCVA), slit-lamp examination and intra-ocular pressure measurement, fundus examination using indirect slit-lamp biomicroscopy to detect the presence of DR and their grading, and to determine the presence or absence of maculopathy. Fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) were done when indicated.

The grading system for DR used in our study was the *National*

*Screening Committee (NSC)* classification and the *International Clinical Diabetic Retinopathy Disease Severity Scale* approved by American Academy of Ophthalmology (Table 1) [8].

**Laboratory investigations:** Apo B (the best marker for dyslipidaemia) was measured by Turbox apo B of Orion Diagnostica Catalogue number 67562.

This was achieved through a quantitative nephelometric determination of apo B in human serum or plasma. It is a liquid phase immuno-precipitation assay with nephelometric end-point detection.

**Statistical analysis:** Data were statistically described in terms of range, mean ± standard deviation (± SD), median frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student $t$ test for independent samples in comparing 2 groups, and the One Way ANOVA for more than 2 groups. Correlation between various variables was done using Pearson's correlation equation for normal variables. $p$ values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for the Microsoft Windows.

## Results

The study was conducted on 168 patients with type II Diabetes Mellitus (DM). The age of the patients ranged from 42 to 70 years old with a mean of 53.59 ± 7.47, with a male: female ratio of 1:5. The duration of DM ranged from 5 to 30 years with a mean of 11.46 ± 5.43. The level of apolipoprotein B (Apo B) ranged from 0.37 to 2.57 g/L with a mean of 1.32 ± 0.48 g/L. The fundus findings in the 168 patients were shown in table 2.

Ninety-three patients had diabetic retinopathy (55.36%) compared to 75 patients without (44.64%). There was a statistically significant increase in apo B in subjects with retinopathy (any degree) as compared to those without retinopathy, using the unpaired t test *(p<0.001)*. Also the correlation between apo B levels and grade of retinopathy, using Pearson's correlation, was statistically significant (r=0.432; *p<0.001*), and also using the One Way ANOVA *(p<0.001)*.

Furthermore, 45 patients had diabetic maculopathy (26.79%) while 123 patients (73.21%) did not. There was a statistically significant increase in apo B in subjects with diabetic maculopathy as compared to those without, using the unpaired t test *(p=0.003)*.

The correlation between apo B levels and the duration of diabetes mellitus was studied and was found to be non-significant by Pearson's correlation (r =-0.063, p=0.415).

## Discussion

Lipoproteins contain a core of hydrophobic lipids surrounded by hydrophilic lipids and proteins (called *apolipoproteins*) that interact with body fluids. The plasma lipoproteins are divided into five major classes based on their relative density: chylomicrons, very low density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs), and high-density lipoproteins (HDLs). Apolipoprotein B (Apo B) is the major structural protein of chylomicrons, VLDLs, IDLs, and LDLs [9].

The use of apo B as a marker of hyperlipidemia is supported by many papers. First, it is the particle which is elevated in diabetic subjects even if the patient is normolipidemic [10]. Second, plasma apo B is an exact measure of the total number of VLDL and LDL particles, so total plasma apo B is a reliable surrogate for LDL particle number [11].

In our study, we found a statistically significant increase in apo B in subjects with retinopathy (any degree) as compared to those without retinopathy *(p<0.001)*, and a fair correlation between apo B levels and grade of DR (r=0.432; *p<0.001*). So, the higher the grade of retinopathy, the higher the apo B level was.

| NSC | International term | American term | Features |
|---|---|---|---|
| *R0* | No DR | *Grade 0* | Normal retina |
| *R1* | Mild NPDR | *Grade 1* | Retinal hemorrhages & microaneurysms |
| *R2* | Moderate NPDR | *Grade 2* | Extensive microaneurysm, retinal hemorrhage, and hard exudates |
| *R2* | Severe NPDR | *Grade 3* | Venous abnormalities, large blot hemorrhages, cotton wool spots, **IRMA**. |
| *R3* | PDR | *Grade 4a* | *NVD or NVE* |
| *R3* | Pre-retinal fibrosis ± tractional RD | *Grade 4b* | Fibrovascular proliferation, RD, preretinal or vitreous hemorrhage, glaucoma |
| *M0* | No maculopathy | | No maculopathy |
| *M1* | Diabetic maculopathy | | **Severe form**:<br>• CSME<br>• Exudative form<br>• Ischemic form<br>**Milder forms:**<br>• Exudate ≤ 1DD of centre of fovea<br>• Circinate or group of exudates within macula<br>• Any microaneurysm or hemorrhage ≤ 1DD of centre of fovea only if associated with BCVA of ≤ 6/12 |
| *P* | Photocoagulation | *Grade 4b* | Small retinal scars throughout the peripheral retina |

BCVA: Best corrected visual acuity; CSME: Clinically significant macular edema; DR: Diabetic retinopathy; DD: Disc diameter; IRMA: Intra-retinal microvascular abnormalities; NPDR: Nonproliferative diabetic retinopathy; NSC: National Screening Committee; NVD: Neovessels of the disc; NVE: Neovessels elsewhere; PDR: Proliferative diabetic retinopathy; RD: Retinal detachment

**Table 1:** Grading of diabetic retinopathy (Wilkinson et al. [8]).

| Grade of DR | 0 | 1 | 1+M | 2 | 2+M | 3 | 3+M | 4 | 4+M | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| No. of patients | 75 | 15 | 9 | 12 | 9 | 3 | 3 | 18 | 24 | 168 |
| Incidence % | 44.64 | 8.93 | 5.36 | 7.14 | 5.36 | 1.79 | 1.79 | 10.71 | 14.29 | 100 |

**Table 2:** Fundus findings.

This was supported by Van Leiden et al. who reported that retinopathy, and hard exudates in retinopathy in particular, were related to elevated serum (LDL) cholesterol levels (apo B is the main component of LDL) [12]. Another study by Deguchi et al. proved that apoB/A-1 ratio may contribute to PDR progression in patients with DR; high apo B and apoB/A-1 values may be related to PDR development [13].

In our work, there was a statistically significant increase in apo B in subjects with diabetic maculopathy as compared to those without (p=0.003). The effect of the duration of diabetes on the apo B levels was also studied. The correlation between apo B levels and duration of diabetes mellitus was found to be non-significant (p=0.415).

Other studies were conducted on the apo A1/B ratio. In a study by Hu et al., they found that low apo A1/apo B ratio in serum was associated with PDR in type II diabetics of long duration [14]. In a study by Romero Aroca et al., apoB/apoA1 ratio was significant to the 10-year incidence of diabetic retinopathy and to macular edema; and the total cholesterol/HDL ratio was significant to a 10-year incidence of macular edema [15].

Finally, we did not consider glycemic control (in the form of normal HbA1c) and this goes with the results of some papers like Taro et al. who found no correlation between glycemic control and concentrations of remnant lipoproteins [16].

Further studies are needed to assess the effect of treatment of apo B on regression of retinopathy.

## Declaration of Interest

## Financial Interest

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