

Research Article

A Study on the Pattern of Lipid Profile and Apolipoproteins in Patients With Diabetic Retinopathy

*¹Vinodhini V.M, ²Gnaneswaran. S, ¹Ebenezer William. W, ³Kumar J.S.,
¹Jeevanathan . A, ¹Poonguzhali D.V.

¹Department of Biochemistry, SRM Medical College Hospital and Research Centre, Tamilnadu, India.

²Department of Ophthalmology, SRM Medical College Hospital and Research Centre, Tamilnadu, India.

³Department of Medicine, SRM Medical College Hospital and Research Centre, Tamilnadu, India.

ABSTRACT

Dyslipidemia is found to be associated with the initiation and progression of diabetic retinopathy (DR). Modifications of lipoproteins by glycation and oxidation and the variations in the size distributions of lipoprotein particles are not reflected in conventional lipid profiles. This study was conducted to know if the measurements of apolipoprotein AI (apo AI) and apolipoprotein B (apo B) may be more directly relevant to the biophysiological changes associated with DR than the traditional lipids. The study subjects consisted of 30 type 2 diabetic patients with DR and 20 type 2 diabetic patients without DR. Diabetic retinopathy was determined by an ophthalmologist using fundoscopic examination. Serum levels of lipids and lipoproteins were measured by standard enzymatic methods. The apo B and apo AI levels did not differ significantly between the two groups. In this study, we did not find any relationship between serum apolipoprotein levels and diabetic retinopathy in type 2 diabetic patients.

Keywords: Apolipoprotein AI, Apolipoprotein B, Diabetic Retinopathy, Type 2 diabetes mellitus.

INTRODUCTION

Hyperlipidemia is a powerful risk factor for atherosclerosis and related disorders such as ischemic heart disease, cerebrovascular diseases and retinal atherosclerosis^(1, 2). The diabetes complications study demonstrated that high triglycerides and high Low Density Lipoprotein Cholesterol (LDL-C) levels at baseline are associated with subsequent progression of retinopathy over 2 years⁽³⁾.

Modifications of lipoproteins by glycation and oxidation and the variations in the size distributions of lipoprotein particles are not reflected in conventional lipid profiles⁽⁴⁾. A study on lipoprotein subclasses by Lyons et al 2004 using Nuclear Magnetic Resonance (NMR) has revealed that more severe diabetic retinopathy was associated with a shift in LDL particle size distribution from large to small⁽⁵⁾.

Diabetic dyslipidemia is characterised by high small dense LDL cholesterol levels⁽⁶⁾. Small dense LDL cholesterol is highly atherogenic due to its ability to penetrate the arterial wall and has low affinity for the LDL receptor⁽⁷⁾.

Apo AI is the major structural protein of High Density Lipoprotein (HDL). Apo B is contained in all the atherogenic lipoproteins namely Very Low Density Lipoprotein (VLDL), Intermediate Density Lipoprotein (IDL), LDL and Lipoprotein (a) [Lp(a)]⁽⁸⁾. Measurement of LDL or VLDL cholesterol may not reflect the actual number of these atherogenic particles whereas the plasma concentration of apo B indicates their cumulative number⁽⁹⁾.

Thus measurements of apo AI and apo B may be more directly relevant to the biophysiological changes associated with diabetic retinopathy than the traditional lipids⁽¹⁰⁾. Hence in the present study we have analysed the lipid profile and apolipoprotein levels in diabetic patients with retinopathy.

MATERIALS AND METHODS

This was a cross sectional study involving 50 Type II diabetic patients of both gender. 30 patients with diabetic retinopathy formed the study group and 20 diabetic patients without diabetic retinopathy served as the control group. All the patients were diagnosed to have type II diabetes mellitus according to the guidelines proposed by American Diabetes Association⁽¹¹⁾. The study was approved by the Institutional Ethical Committee and informed consent was obtained from all the participants. After 12 hrs of fasting, plasma glucose and serum lipid profile were measured by Beckman Coulter auto analyser using enzymatic kits. Serum apo B and apo AI levels were measured by immunoturbidimetric method by Beckman Coulter auto analyser. Fundoscopic examination was performed through dilated pupils by an experienced ophthalmologist.

STATISTICAL ANALYSIS

Variables were compared between control and study groups by using the students unpaired 't' test. All probability values presented are two tailed and probability values <0.05 were considered to be statistically significant.

Table I: Clinical and laboratory characteristics of the control and study groups: All the values are expressed as Mean \pm SD

Parameters	Control group	Study group	p value
No. of cases(n)	20	30	
apo (A I)(mg/dl)	131.75 \pm 2.5	126.4 \pm 2.6	NS
apo (B)(mg/dl)	102.9 \pm 10.5	102.13 \pm 4.2	NS
Cholesterol (mg/dl)	201 \pm 8.9	172.4 \pm 9.5	Significant
Triglycerides (mg/dl)	165.4 \pm 16.5	138.7 \pm 13	NS
High Density Lipoprotein -C(mg/dl)	40.2 \pm 1.8	38.86 \pm 1.8	NS
Low Density Lipoprotein-C(mg/dl)	127.5 \pm 7.03	107.1 \pm 7.9	NS
Very Low Density Lipoprotein-C (mg/dl)	33.2 \pm 3.3	27.3 \pm 2.8	NS

SD – Standard Deviation, NS – Non Significant.

RESULTS

The mean level of apo AI was decreased in the DR group when compared with the control group, but the difference was not statistically significant. Similar results were obtained for HDL cholesterol. There was no significant difference between apo B levels in both the groups. Clinical and laboratory characteristics of the control and study groups are presented in Table I.

DISCUSSION

Dyslipidemia is associated with initiation and progression of diabetic retinopathy⁽¹²⁾. The apolipoproteins are protein moieties with structural, enzymatic and receptor binding functions⁽⁸⁾. Therefore in the present study we have analysed the levels of apolipoprotein AI and B in patients who have developed diabetic retinopathy. Apo AI has anti-inflammatory and antioxidant effects and is involved in intra-retinal lipid transport⁽¹³⁾. Low levels of apo AI may thus promote diabetic retinopathy⁽¹⁶⁾.

In the present study, a decrease in apo AI levels has been observed in the diabetic retinopathy group, although no significant difference was observed between the apo AI levels of the two groups.

Similarly Yuzo et al (2009) have reported low levels of apo AI in patients with diabetic retinopathy⁽¹⁴⁾. Higher apo B levels which may reflect higher lipoprotein related toxins are destructive to arterial and retinal vascular cells⁽¹⁵⁾. Sasongko et al (2011) have demonstrated apo AI, apo B and apo B to apo AI ratio to be significantly associated with diabetic retinopathy and its severity⁽¹⁶⁾. But in the present study, apo B levels were not statistically significant between the two groups. These findings could be due to variations in the severity of diabetic retinopathy among the participants, moreover the control group comprised of patients with type 2 diabetes.

Wu et al (2008) have reported that the frequency of expression of apo B-100 in retina increased in proportion to the severity of diabetic retinopathy⁽¹⁵⁾. But Simo et al (2009) have found excessive apo AI in the retina of patients with early stage of diabetic retinopathy. They suggested that more lipids may accumulate within the retina in patients with a lower capacity for apo AI production in the retina, resulting in progression of diabetic retinopathy⁽¹⁷⁾. The regulatory mechanism of lipid deposition to and from target tissues particularly the retina may be more than the concentration of total

cholesterol in the pathogenesis of diabetic retinopathy^(15, 17, 18, 19).

Conflicting results have been reported about the serum total cholesterol concentrations in patients with diabetic retinopathy. Studies carried out with type 2 diabetic patients having diabetic retinopathy have reported significantly elevated concentrations of total cholesterol^(20, 21). On the contrary, other studies showed that the mean levels of lipids were not significantly different in patients with diabetic retinopathy^(16, 22, 23).

The major limitation of this study was the small size of the study groups. There was widespread use of statins in both the study and control groups. Studies involving a larger patient population may help to know if these apolipoprotein measurements can be considered to be better biomarkers of diabetic retinopathy than the traditional lipid measures.

CONCLUSION

In conclusion in this study we did not find any relationship between serum apolipoprotein levels and diabetic retinopathy in type 2 diabetic patients.

REFERENCES

1. Wilkinson I, Cockcroft JR. Cholesterol, lipids and arterial stiffness. *Adv Cardiol* 2007; 44:261-277.
2. Tedeschi-Reiner E, Reiner Z, Sonicki Z. Atherosclerosis of retinal arteries in men: role of serum lipoproteins and apoproteins. *Croat Med J* 2004;45:333-337.
3. Orchard TJ, Dorman JS, Maser RE, et al. Factors associated with avoidance of severe complications after 25 yr of IDDM. Pittsburgh Epidemiology of Diabetes Complications Study I. *Diabetes Care*. 1990;13:741-747.
4. Lyons TJ, Jenkins AJ. Glycation, oxidation and lipoxidation in the development of the complications of diabetes: a carbonyl stress hypothesis. *Diabetes Rev*. 1997; 5:365-391.
5. Timothy J. Lyons, Alicia J. Jenkins, Deyi Zheng, Daniel T. Lackland, Daniel McGee, W. Timothy Garvey, Richard L. Klein, and The DCCT/EDIC Research Group. Diabetic Retinopathy and serum lipoprotein subclasses in the DCCT/EDIC Cohort. *Investigative Ophthalmology & Visual Science* 2004;45 (3):916-918.

6. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. *Nat Clin Pract Endocrinol Metab.* 2009; 5(3):150-159.
7. Koba S, Yokota Y, Hirano T, Ito Y, Ban Y, Tsunoda F: Small LDLC-cholesterol is superior to LDLC-cholesterol for determining severe coronary atherosclerosis. *J Atheroscler Thromb* 2008, 15(5):250-260.
8. Marcovina S, Packard CJ. Measurement and meaning of apolipoprotein AI and apolipoprotein B plasma levels. *J Intern Med* 2006;259:437-446.
9. Fathima Hussain Kanani, Junaid Mehmood Alam : Apolipoprotein B in type 2 diabetics – a cross sectional study in a tertiary care set-up. *J Pak Med Assoc* 2010; 60(8):653-656.
10. Davidson MH. Apolipoprotein measurements: Is more widespread use clinically indicated? *Clin Cardiol* 2009;32:482-486.
11. American Diabetes Association: Clinical practice recommendations 2000. *Diabetes care* 2000;23:345-355
12. Klein R, Sharrett AR, Klein BE, et al. The association of atherosclerosis, vascular risk factors and retinopathy in adults with diabetes : the atherosclerosis risk in communities study. *Ophthalmology* 2002;109:1225-1234.
13. Tserentsoodol N, Gordiyenko NV, Pascual I, Lee JW, Fliesler SJ, Rodriguez IR. Intraretinal lipid transport is dependent on high density lipoprotein-like particles and class B scavenger receptors. *Mol Vis* 2006;12:1319-1333
14. Yuzo Deguchi, Takatoshi Maeno, Yoshitsugu Saishin, Yuichi Hori, Tomoaki Shiba, and Mao Takahashi. Relevance of the serum Apolipoprotein Ratio to Diabetic Retinopathy. *Jpn J Ophthalmology* 2011;55:128-131.
15. Wu M, Chen Y, Wilson K, et al. Intraretinal leakage and oxidation of LDL in Diabetic Retinopathy. *Invest Ophthalmol Vis Sci* 2008;49:2679-2685.
16. Muhammad Bayu Sasonko, Tien Y. Wong, Thanh T. Nguyen, Ryo Kawasaki, Alicia Jenkins, Jonathan Shaw, Jie Jin Wang. Serum apolipoprotein AI and B are stronger biomarkers of diabetic retinopathy than traditional lipids. *Diabetes Care* 2011;34:474-479.
17. Simo R, Garcia-Ramirez M, Higuera M, et al. Apolipoprotein AI is overexpressed in the retina of diabetic patients. *Am J Ophthalmol* 2009;147:319-325.
18. Simo R, Higuera M, Garcia- Ramirez M, Canals F, Garcia-Arumi J, Hernandez C. Elevation of apolipoprotein AI and apolipoprotein H levels in the vitreous fluid and overexpression in the retina of diabetic patients. *Arch Ophthalmol* 2008; 126:1076-1081.
19. Simo R, Hernandez C. Advances in the medical treatment of diabetic retinopathy. *Diabetes Care* 2009;32:1556-1562.
20. U G O Ergun MD, S Oztunzun MD, G Seydaoglu MD : Lipoprotein (A) levels in type 2 diabetic patients with diabetic retinopathy. *Med J Malaysia* 2004; 59 (3):406-410.
21. Amir Ghorbanihaghjo, Alireza Javadzadeh, Hassan Argani, Nariman Nezami, Nadereh Rashtchizadeh, Mandana Rafeey, Mohammad Rohbaninoubar, Babak Rahimi-Ardabili : Lipoprotein (a), Homocysteine, and retinal arteriosclerosis. *Molecular Vision* 2008;14 : 1692-1697.
22. Rupali Chopra, MS; Jaison G Saramma, MS; John Mary, MD; Abraham Rebecca, PhD : Lipoprotein (a) as a risk factor for diabetic retinopathy in patients with diabetes mellitus. *Indian Journal of Ophthalmology* 2012;55(3):195-198.
23. Chul-Hee Kim MD, Hyung-Joo Park MD, Joong-Yeol Park MD, Sung-Kwan Hong MD, Young-Hee Yoon MD, Ki-Up Lee MD: High serum lipoprotein(a) levels in Korean type 2 diabetic patients with proliferative diabetic retinopathy. *Diabetes Care* 1998; 21(12): 2149-2151.