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Serum Lipids and Apolipoproteins in Diabetic Retinopathy: A Case Control Study

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Abstract:
Aim*: To evaluate association of apolipoproteins A1 and B and fasting lipid profile (FLP) with diabetic retinopathy (DR) in adults.*
Materials and Methods: *This is a hospital based 9 months case control study of diabetic subjects (n= 169) by Ophthalmological examination and Biochemical parameters (Fasting plasma glucose (FPG), FPL , Apolipoproteins A1 and B) .Statistical analysis was done using SPSS version 17.*
Results*: Out of 169 diabetic subjects studied(mean age - 55.46±9.78 years; mean BMI - 24.25±3.71; Mean duration of diabetes - 10.17±7.45years) , 51.5% (87/169) had no signs of DR, 11.8% (20/169) had mild NPDR, 16.6% (28/169) had moderate NPDR, 6.5% (11/169) had severe NPDR and 13.6% (23/169) had proliferative DR. FPG (p-0.02), TC (p-0.009), LDL-C (p-0.053), HDL-C (p-0.001) and TG (p-0.0001) were found to have a statistically significant association with DR. ApoA1 (OR-0.996 and p-0.393) and apo B (OR-1.006 and p-0.145) showed no statistically significant association with DR apo B /Apo A1 ratio (OR-2.11 and p-0.048) showed a statistically significant association with DR. No significant correlation was observed between various lipid parameters and apolipoproteins with different stages of diabetic retinopathy.*
Conclusion*: The significant association of serum lipids and Apolipoprotein B/apo A-1 ratio with DR shown by this study indicates, along with glycemic control, correction of hyperlipidemia is important in preventing the development of DR. Besides, the Apo B / apo A -1 ratio can be used as an index of DR.*
Keywords*: Diabetic retinopathy, Serum Lipids, Apolipoprotein A1, Apolipoprotein B, Apolipoprotein B/ apo A-1 ratio (apo B/apo A-1 ratio*)

I. Introduction

Diabetic retinopathy (DR) is a common, specific microvascular complication of diabetes mellitus (DM) causing visual impairment which is preventable by screening and clinical management. A positive association has been shown between DR and duration of DM, poor glycemic control [1] and unhealthy lipid profile [2] . Recently apolipoprotein A1 (apo A-1) of antiatherogenic HDLand apolipoprotein B (apo B) of atherogenic LDL are found relevant to biophysiological changes of DR than traditional lipids. [3, 4, 5] There is an increasing prevalence of type 2 DM and DR in India. [6,7] Type 2 DM in Indians differ from the West in different aspects [2,4] indicating the importance of regional studies.

Aim

To evaluate and compare the association of apo A -1 , apo B and traditional lipid profile with diabetic retinopathy in adults with type 2 DM.

II. Materials and Methods

This was a hospital-based case-control study. The study group consisted of 169 type 2 DM patients who attended the Medicine OPD and/ or Retina Clinic of Government Medical College, Thrissur, from April 2012 to December 2012. Patients diagnosed with DR of any stage were taken as cases and type 2 DM patients without any evidence of retinopathy were taken as controls of this study.

Inclusion criteria: Type 2 DM patients with and without DR.

Exclusion Criteria: Type 2 DM patients with history of glaucoma, liver disease, previous vitreoretinal surgery and those with media opacity were excluded from the study.

Clinical Assessment: Clinical and treatment history, family history of having at least one first degree relative diagnosed of type 2 DM and demographic data were collected, and a complete physical examination was done. Diagnosis of type 2 DM was made according to WHO criteria. [8] A complete ophthalmological examination was performed including fundus examination with slit lamp biomicroscopy and indirect ophthalmoscopy, fundus colour photograph centered on the macula and fundus fluorescein angiography wherever indicated;

subsequently subjects were classified as cases (with DR) and controls (without DR). Cases were further divided into non-proliferative DR and proliferative DR, in which non proliferative DR was sub stratified into mild NPDR, moderate NPDR, severe NPDR and very severe NPDR according to the International Clinical Diabetic Retinopathy Disease Severity Scale. [9] The worse eye was used to determine the severity scale of a patient.

Anthropometric Measurements: Participants were weighed in light clothing without shoes and their heights measured. Body mass Index (BMI) was calculated as kilogram per meter square (kg/m^2).

Biochemical Analysis: Blood samples were collected after overnight fasting (> 8 hours) by venipuncture. Estimation of FPG (fasting plasma glucose) done by glucose oxidase - peroxidase based method and serum lipid profile (Total cholesterol – CHOD – PAP method; Triglycerides – GPO – PAP method, HDL – Cholesterol (HDL – C) – indirect method by selective precipitation of low density lipoprotein cholesterol by phosphotungstate and $MgCl_2$) was carried out using EM 360 Autoanalyser (Transasia) utilizing kits provided by Agappe diagnostics. LDL cholesterol (LDL-C) was calculated using the Friedewald formula. Serum apo A - 1 and apo B were measured by immune turbidimetry (Quantia).

Ethics: A written consent was obtained from each participant and the study was approved by Institutional Ethics Committee (IEC), Government Medical College, Thrissur, Kerala.

Statistics: Data analysis was performed with SPSS version 11.5. Baseline characteristics of participants with or without DR were compared using Chi-square test and t-test. Logistic regression was used to calculate adjusted odds ratio between serum lipids and apolipoproteins with DR.

III. Results:

General characteristics of study population: The diabetic patients (n=169) of this case control study showed mean age 55.46±9.78 years, BMI 24.25±3.71 and duration of type 2 DM 10.17±7.45 years. Out of 169 subjects 51.5% (87) had no signs of DR, 11.8% (20) had mild NPDR, 16.6% (28) had moderate NPDR, 6.5% (11) had severe NPDR and 13.6% (23) had proliferative DR. Analysis of various parameters of the study subjects are shown in Table 1.

Association of serum lipids and DR: Logistic regression analysis showed statistically significant association of FPG, Total Cholesterol, LDL- C, HDL- C and TG with DR. ApoA1 and B were found to differ considerably in patients with and without DR, but the differences were not statistically significant. However, apo B/apo A-1 ratio showed a statistically significant correlation with DR**.** (Table 1 and 2)

Association between serum lipids and stages of retinopathy: No statistically significant correlation was observed between various lipid parameters – both conventional lipid profiles and apolipoproteins with different stages of DR as shown in Table 3.

Association of various risk factors to development of DR: Family history of diabetes, hypertension, and smoking were found to be significantly related to the development of DR as shown in Table 4.

IV. Discussion

The aim of our study was to find out the association between serum lipids and apo A -1 and apo B with DR and this study showed statistically significant association of FPG (high levels) (see table 1), serum lipids (high total Cholesterol, high TG, and low HDL - C) and apo B/apo A-1 ratio (high) with DR. But there was no statistically significant independent association of apolipoprotein A - 1 and B with DR. These results are consistent with several other studies. [**1,2,7,10,11,12,13,14].** But in a recent study , Sasongko et al [3] reported statistically significant association between apo A1, apo B and apo B/apo A-1 ratio with DR.

The finding of significant association of apo B/apo -1 ratio and the lack of significant independent association of these apolipoproteins with DR supports the following concepts. Apo A-1 has anti-inflammatory and antioxidant actions [19.,20,21] and in addition it specifically inhibits oxidation of LDL to form oxidized LDL. The oxidized LDL will deteriorate antiplatelet and anti-inflammatory functions of endothelium. Hence we need a parameter that reflect the net effect produced from the interactions of apo A-1 and apo B which seems to be crucial in the pathogenesis of microangiopathy leading to DR. For that apo B/apo A-1 ratio will be useful and was proved by our study as well as several other studies [**1,3,14,15]**.

In Sasongko MB et al study **[15]** ,the apo B/apo A-1 ratio indicated association between measures of vascular functions like flicker light induced retinal arterial dilatation and retinal arterial tortuosity suggestive of its role in retinal microvasculature. Their study also showed significant differences between apo A1 and apo B with different stages of diabetic retinopathy. But in our study, there was no significant independent association of apo A1 and apo B with DR.

No significant association was found between either serum lipids or apolipoproteins with the severity of diabetic retinopathy in our study. But in DCCT/EDIC **[10]**, a study in a type 1 diabetic population, there was a positive association of TG and an inverse association of HDL-C with severity of DR, but no significant association was noted with total cholesterol (TC). In the CURES study, TC was found to be an independent risk factor for DR **[7]**. Sasongko et al [3] also established inverse association of HDL–C with any type of DR.

WESDR (Wisconsin Epidemiologic Study of Diabetic Retinopathy) [12] and a cross-sectional study from Bangalore [16] did not show any association between dyslipidemia with occurrence or severity of DR. No association was found between serum lipids and progression of DR in type 2 DM in the FIELD study [17]. According to Deguchi et al apoA1 ,apo B and apo B/ apo A-1 ratio are related to the development of Proliferative DR (p value 0.08, 0.02 and 0.004 respectively) [14]. Another study by Andina Hu et al also showed significant association between apolipoprotein ratio and proliferative DR[1].

Our study noted statistically significant association between family history of type 2 DM and DR. The DCCT study [10] reported familial clustering of DR (odds ratio of 5.4) in diabetic relatives of diabetic retinopathy subjects compared to those without retinopathy [18]. Both smoking and presence of hypertension were also significantly associated with DR. (see table 4)

Present study once again reaffirms high TC, high TG , low HDL -C, high LDL- C ,high apo B /apo A-1 ratio and family history of diabetes as potential risk factors of DR and hence the need of tight control of diabetes and lipid profile by diet, life style modifications and drugs to lessen or prevent the occurrence of DR. It also alert the need of optimum control of hypertension, quit the habit of smoking as these factors showed significant association with DR. In addition it lights up the potential of apo B /apo A-1 ratio as a marker of DR.

Our study has some limitations. 1)The study determined the scale of diabetic retinopathy based on clinical examination rather than from standard fundus photographs (2) Sample size may not be enough in various stages of retinopathy, to assess the relation of serum lipids and apolipoproteins with the severity of retinopathy (3)Direct methods of assay for LDL and HDL could have given a better estimate of these lipoproteins than the indirect methods used in this study (4) Since the study was hospital based it may not reflect the true status of all diabetic patients in the population. (5) This study showed a statistically significant association between apo B/apo A-1 ratio with diabetic retinopathy which indicates the need for doing a similar study with larger sample size to unravel the independent association of apo B and apo A - 1 with DR.

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References

[1]. Andina Hu,Yan Luo,Tao Li,Xiaobo Guo,Xiaoyan Ding,Xiaobo Zhu et al.Low serum apolipoprotein A1/B ratio associated with proliferative diabetic retinopathy in type 2 diabetes. Grefes Arch Clin Exp Ophthalmol 2012;250:957-962

[2]. Rema M,Premkumar S,Anitha B,Deepa R,Pradeepa R,Mohan V.Prevalence of diabetic retinopathy in urban India:The Chennai Urban Rural Epidemiology Study(CURES) Eye Study, Ⅰ. Invest Ophthalmol Vis Sci,2005;46:2328-2333

[3]. Sasongko MB,Wong TY,Nguyen TT , Kawasaki R,Jenkins A, Shaw J,et al .Serum apolipoprotein AI and B are stronger biomarkers of diabetic retinopathy than traditional lipids. Diabetes Care 2011;34:474–479

[4]. Chait A,Montes VN. Apolipoproteins and diabetic retinopathy. Diabetes Care 2011;34:529-531

[5]. Engerman RL.Pathogenesis of diabetic retinopathy.Diabetes.1989;38:1203-1206

[6]. Narendran V,John RK,Raghuram A,Ravindran RD,Nirmalan PK,Thulasiraj RD,Diabetic retinopathy among self reported diabetics in southern India: a population based assessment. Br J Ophthalmol 2002;86:1014-1018

[7]. Rema M,Srivatava BK,Anitha B,Deepa R,Mohan V. Association of serum lipids with diabetic retinopathy in urban south Indians-the Chennai Urban Rural Epidemiology Study(CURES) Eye Study,Ⅱ, Diabet Med 23:1029-1036

[8]. World health organization: Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation,2006

[9]. Wilkinson CP,Ferris FL,Klein RE,Lee Paul P, et al, Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology - September 2003 .Vol. 110, Issue 9, Pages 1677-1682

[10]. Lyons TJ,Jenkins AJ,Zheng D,Lackland DT,McGee D,Garvey WT et al.Diabetic retinopathy and serum lipoprotein subclasses in the DCCT/EDIC cohort. Invest Ophthalmol Vis Sci 2004;45:910-918

[11]. Zhang H, Wang J,Ying G,Shen L,Zhang Z.Serum lipids and other risk factors for diabetic retinopathy in Chinese type 2 diabetic patients.J Zhejiang Univ-Sci 2013,14(5):392-399

[12]. Klein BE,Moss SE,Klein R,Surawicz TS.The Wisconsin Epidemiologic Study of Diabetic Retinopathy,XⅢ. Relationship of serum cholesterol to retinopathy and hard exudates.Ophthalmology 1991:981261-5

[13]. Adinortey MB, Gyan BE, Adjimani J, Nyarko P, Sarpong C,Tsikata F,et al. Dyslipidemia associated with type 2 diabetics with micro and macrovascular complications among Ghanaians. Ind J Clin Biochem,2011;26(3):261-268

[14]. Deguchi Y,Maeno T,Saishin Y, Hori Y, Shiba T,Takahashi M. Relavance of serum apolipoprotein Ratio to diabetic retinopathy. Jpn J Ophthalmol 2011;55:128-131

[15]. Sasongko MB,Wong TY,Nguyen TT,Kawasaki R,Jenkins A,Shaw J,et al. Serum Apolipoproteins Are Associated With Systemic and Retinal Microvascular Function in People With Diabetes . Diabetes 2012; 61:1785-1792

[16]. Jyothi I,Suneetha N,Mary J, Ajoy Mohan VK, Usha Vasu,Sadiqet M.Serum lipids and diabetic retinopathy:A cross sectional study. Indian J Endocrinol Metab.2012;16:S492-S494

[17]. Keech AC,Mitchell P,Summanen PA,O'Day J,Davis TME,Moffitt MS et al.Effect of fenofibrate on the need for laser treatment for diabetic reinopathy(FIELD study):a randomized controlled trial. Lancet 2007;370:1687-1697

[18]. The Diabetes Control and Complication trial Research Group. Clustering of long term complications in families with diabetes in the diabetes control and complication trial. Diabetes.1997.;46:1829-1839
[19]. Shah PK, Kaul S, Nilsson J, Cercek B. Exploiting the vascular protective effects of high-density lipoprotein and its apolipoproteins: an idea whose time for testing is coming, part II. Circulation 2001;104:2498–2502
[20]. Davidson MH. Apolipoprotein measurements: is more widespread use clinically indicated? Clin Cardiol 2009;32:482–486
[21]. Marcovina S, Packard CJ. Measurement and meaning of apolipoprotein AI and apolipoprotein B plasma levels. J Intern Med 2006;259:437–446

Table 1 .General characteristics of study population

	No DR (Mean ±SD)	With DR (Mean ±SD)	Mean difference	P value
Age	55.01 ±9.79	55.93±9.8	-0.915	0.545
BMI	24.24±4.41	23.25±2.71	0.985	0.084
FPG	152.51±61.08	173.23±53.175	-20.726	0.020
TC	185.5±48.03	210.6±54.03	-2.509	0.002
LDL-C	101.24±44.46	126±48.25	-25.283	0.001
HDL-C	62.57±19.07	55.13±15.24	7.441	0.006
TG	129.33±53.997	164.77±63.36	-35.44	0.000
ApoA1	143.92±33.14	138.98±35.36	4.944	0.350
Apo B	115.82±37.88	125.38±43.69	-9.556	0.130
Apo B/Apo A1	0.853±0.36	0.974±0.44	-0.121	0.054

(DR-Diabetic retinopathy, SD-standard deviation, BMI-body mass index, FPG-fasting plasma glucose, TC : Total cholesterol, LDL-C --low density lipoprotein cholesterol, HDL-C -- high density lipoprotein cholesterol, TG-triglycerides, Apo A1-apolipoprotein A1, Apo B-apolipoprotein B)

Table 2. Association of serum lipids and retinopathy

	Adjusted Odds ratio (95% CI)	P value
Apo A1	0.996 (0.991 – 1.001)	0.393
Apo B	1.006 (1.002 - 1.010)	0.145
Apo B-Apo A1 ratio	2.110 (0.703 - 3.520)	0.048
TC	1.043 (1.026 - 1.059)	0.009
LDL	0.968 (0.951 - 0.984)	0.053
HDL	0.939 (0.921 - 0.957)	0.001

(LDL-C --low density lipoprotein cholesterol, HDL-C -- high density lipoprotein cholesterol, Apo A1-apolipoprotein A1, Apo B-apolipoprotein B)

Table 3. Association between serum lipids and stages of retinopathy

	Adjusted Odds ratio (95% Confidence Interval for OR)	
	No DR Vs NPDR	NPDR Vs PDR
Apo A1	1.010 (0.997-1.024)	1.009 (0.995-1.023)
Apo B	0.989 (0.978-0.999)	0.992 (0.981-1.002)
Apo B / A-1 ratio	0.206 (0.071-0.595)	0.291 (0.097-0.873)
TC	0.952 (0.914-0.981)	0.989 (0.954-1.025)
LDL	1.040 (0.996-1.087)	1.009 (0.970-1.050)
HDL	1.094 (1.039-1.152)	1.037 (0.988-1.089)

(DR-Diabetic Retinopathy, NPDR – Non-Proliferative Diabetic Retinopathy, PDR – Proliferative Diabetic Retinopathy, LDL-C --low density lipoprotein cholesterol, HDL-C -- high density lipoprotein cholesterol, Apo A1-apolipoprotein A1, Apo B-apolipoprotein B)

Table 4. Association of various risk factors to development of retinopathy

Risk factors	Odds Ratio	95% Confidence Interval
Family history of Diabetes(+/-)	1.846	0.999 - 3.409
History of hypertension(+/-)	2.717	1.444 - 5.11
Smoking(+/-)	2.105	1.016 - 4.361