Journal of Research in Medical Education & Ethics
Vol. 5, No. 3, November, 2015, pp-220-226

DOI: 10.5958/2231-6728.2015.00045.1

ORIGINAL RESEARCH

Association of Lipid Profile with Severity of Retinopathy in Patients with Type-2 Diabetes Mellitus

Mitali Srivastava[1], Annapurna Kumar[2]*, Sumathi S[3]
*Corresponding author email id: annapurna200@gmail.com

ABSTRACT

Background: Diabetic retinopathy is a leading cause of visual morbidity. Duration of diabetes, hypertension and poor glycaemic control are known risk factors for retinopathy. However, the role of dyslipidemia is less clear as various studies give conflicting results. **Aim:** To determine the association of serum lipids with retinopathy in patients with type-2 diabetes mellitus. **Settings and design:** This was a cross-sectional study conducted on patients with type-2 diabetes mellitus presenting to the ophthalmology outpatient department. **Methodology:** About 100 patients with type-2 diabetes mellitus with a normal BMI were examined for retinopathy. The patients were divided into diabetics without retinopathy, mild non-proliferative diabetic retinopathy (NPDR), moderate NPDR and severe NPDR. HbA1c, fasting blood glucose and fasting lipid profile were evaluated. **Statistical analysis:** Descriptive statistics were followed by an unpaired *t*-test to compare the groups. Pearson's test was used to assess the nature of correlation between the study population and variables. A *p* value of <0.05 was considered significant. **Results:** Age, duration of diabetes, systolic and diastolic blood pressure correlated significantly with severity of retinopathy. Laboratory parameters showing a significant correlation with severity of retinopathy were fasting blood sugar= 0.480 ($p<0.001$, glycated haemoglobin $r= 0.460$ ($p<0.001$), triglycerides $r= 0.279$ ($p= 0.005$), total cholesterol $r= 0.246$ ($p=0.014$), LDL, $r= 0.238$ ($p=0.017$) and VLDL, $r= 0.292$ ($P= 0.003$). HDL correlated negatively with retinopathy ($r=$ "0.038) but was not significant. **Conclusion:** Serum lipids excepting HDL were found to have a significant correlation with the presence of and severity of diabetic retinopathy.

Keywords: Lipids, Diabetic retinopathy, Visual morbidity, Lipid profile, Microvascular complications

INTRODUCTION

Diabetic retinopathy is one of the microvascular complications of diabetes mellitus and is a leading cause of new cases of blindness in adults[1]. The prevalence of diabetic retinopathy varies in different studies based on the study design and selection criteria. Population-based studies that have included both known and newly diagnosed patients with diabetes mellitus show lower rates of prevalence of diabetic retinopathy in the Indian as compared to that of the western population. Rema *et al*.[2] in the Cures eye study found a prevalence rate of 17.6% and the Aravind comprehensive eye study[3] 10.5%. This is in contrast to the higher figures found in Western studies such as 36.8% in the Beaver dam eye study[4], 32.4% in the blue mountains eye study[5] and 20.5% in the atherosclerosis risk in communities study[6]. The Wisconsin epidemiologic study of diabetic retinopathy found a prevalence of retinopathy to range from 28.8% to 77.8% depending on the duration of diabetes[7].

Prolonged duration of diabetes, hypertension and poor glycaemic control have been shown to be related to diabetic retinopathy[7–9]. However, there is less agreement as to the association of dyslipidemia with that of retinopathy. Agrawal *et al*.[10] found LDL to

[1]Postgraduate Student, [3]Professor and Head, Department of Biochemistry, Sri Manakula Vinayagar Medical College and Hospital, Pondicherry University, Pondicherry, India
[2]Professor and Head, Department of Ophthalmology, Karpaga Vinayaga Institute of Medical Sciences, Tamil Nadu Dr. M.G.R. Medical University, Tamil Nadu, India

be associated with diabetic retinopathy whereas Agroiya *et al*.[9] found a similar association for both low density lipoproteins and triglycerides. Other studies[11–14] however did not find any difference in lipid levels in patients with various stages of retinopathy. Hence, this study was undertaken to determine the association of lipid levels with retinopathy, and the nature of this association in our hospital.

MATERIALS AND METHODS

This cross-sectional study was undertaken on patients who were seen in the department of ophthalmology. The study was approved by the Institutional Ethics Committee and conformed to the tenets of the declaration of Helsinki. A written informed consent was obtained from all patients.

One hundred patients diagnosed with type-2 diabetes mellitus were enrolled in this study. A complete history was obtained and ocular examination was carried out for all patients. A dilated fundus examination with a Goldmann three mirror fundus contact lens was done in all patients. Patients with retinopathy were grouped into mild non-proliferative diabetic retinopathy (NPDR), moderate and severe NPDR based on early treatment diabetic retinopathy study (ETDRS) guidelines[15]. None of the patients in this study had proliferative retinopathy. A general clinical examination including blood pressure was recorded. Body mass index (BMI) was calculated as weight in kilograms divided by square of height in meters (kg/m^2).

The patients were divided into the following groups: group A diabetics without NPDR, group B mild NPDR, group C moderate NPDR and group D severe NPDR. Patients with a BMI of $\leq$18 or $\geq$25 kg/m^2 and those in whom fundus could not be visualised were excluded from the study. Blood samples for laboratory parameters were collected.

Estimation of HbA1c

Glycated haemoglobin was measured using the coral biosystems glycated haemoglobin kit ion exchange resin method. The test was done following standardisation in the hospital's biochemistry laboratory.

Estimation of Serum Lipids and Fasting Blood Glucose

Serum total cholesterol (TC) was measured by the cholesterol oxidase–peroxidase method, triacylglycerol (TG) levels by cholesterol oxidase–peroxidase method and high density lipoproteins (HDL) by divalent cation precipitation method. Low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) were calculated by Friedwald's formula where VLDL was calculated as Triglyceride/5, and LDL was taken as total cholesterol-HDL + VLDL[16]. Fasting blood glucose FBG was measured by the glucose oxidase–peroxidase method. All these methods were analysed using Cobas Mira plus Automated Chemistry Analyzer, USA.

Statistical Analysis

Parameters were presented as mean ± standard deviation. The data were analysed using SPSS software version 11.5. Descriptive statistics were followed by an unpaired *t*-test that was used to compare the groups with and without diabetic retinopathy. Pearson's test was used to assess the nature of correlation between the study population and the variables. A p value of <0.05 was considered significant.

RESULTS

One hundred diabetic patients were part of this study. The mean age of the patients was 56.86 ± 10.14 with a range of 34–78 years. The patients consisted of 59 males and 41 females. Table 1 shows the distribution of patients and Table 2 shows the clinical and biochemical characteristics in the various study groups.

Age and duration of diabetes correlated strongly with increasing severity of retinopathy $r = 0.253$, $p = 0.011$ and $r = 0.401$, $p < 0.001$, as did both systolic and diastolic

Table 1: Distribution of patients in the various study groups

	No retinopathy Group A	Mild retinopathy Group B	Moderate retinopathy Group C	Severe retinopathy Group D
Number of patients (*N*)	32	24	26	18

Table 2: Clinical and biochemical characteristics of the study groups

	No retinopathy Group A	Mild retinopathy Group B	Moderate retinopathy Group C	Severe retinopathy Group D	*r*	*P*
Age (years)	55.22±10.44	52.75±9.6	59.69±10.86	61.17±6.45	0.253	0.011
Duration (years)	2.98±2.72	6.12±5.06	6.90±5.42	8.61±5.03	0.401	<0.001
SBP (mmHg)	116.81±8.45	121.67±9.81	126.85±17.73	129±9.39	0.373	<0.001
DBP (mmHg)	74.56±7.79	80.92±8.34	83±10.93	87.22±6.86	0.465	<0.001
FBS (mg/dl)	125.09±43.69	141.08±51.74	177.81±54.77	202.44±71.73	0.480	<0.001
HbA1c (%)	7.45±0.92	8.36±0.76	7.9±0.79	8.97±0.6	0.460	<0.001
TC (mg/dl)	179.78±30.21	185.79±31.08	190.92±60.51	214.72±53.96	0.246	0.014
TG (mg/dl)	121.06±56.19	137.79±69.32	147.27±78.39	183.72±91.01	0.279	0.005
HDL (mg/dl)	37.78±4.77	40.46±6.03	38.58±7.21	37.05±8.18	-0.038	0.706
LDL(mg/dl)	111.91±29.53	117.79±29.14	124.15±47.74	138.61±43.82	0.238	0.017
VLDL (mg/dl)	22.81±9.1	27.96±13.61	28.31±13.06	34.39±15.63	0.292	0.003

BP, blood pressure; FBS, fasting blood sugar; HbA1c, glycated haemoglobin; TC, total cholesterol; TG, triglycerides; HDL, High density lipoprotein; LDL, Low density lipoprotein; VLDL, Very low density lipoprotein.

blood pressures with $r = 0.373$, $p < 0.001$ and $r = 0.465$, $p < 0.01$, respectively.

Laboratory parameters which were found to have a strong positive correlation with severity of retinopathy were fasting blood sugar $r = 0.480$, $p<0.001$, glycated haemoglobin $r=0.460$, $p<0.001$, total cholesterol $r = 0.246$, $p = 0.014$, triglycerides $r=0.279$, $p=0.005$, LDL cholesterol $r=0.238$, $p=0.017$ and VLDL $r = 0.292$, $p = 0.003$. HDL cholesterol correlated negatively with severity of retinopathy but was not significant $r = -0.038$, $p = 0.706$. A general trend towards poor HDL cholesterol levels were noted in the entire study population, with a mean HDL value of 38.33±3.99 mg/dl.

DISCUSSION

Dyslipidemiais strongly linked to the presence of diabetes. Diabetic dyslipidemia refers to an abnormal lipoprotein profile associated with insulin resistance, where elevated triglycerides and LDL along with reduced HDL concentrations are found[17]. Various studies have observed a positive association of retinopathy with total cholesterol[8,18] and triglycerides[9,10,18–22].

The role of dyslipidemia in diabetic retinopathy is speculated to have several mechanisms. Elevated serum lipids lead to reduced bioavailability of nitric oxide (NO). Nitric oxide is involved in endothelium-dependent vasodilation, regulation of leukocyte adhesion and infiltration and inhibition of platelet adhesion and aggregation. These events in turn lead to microvascular alterations[23]. Another pathway by which lipids may contribute to microvascular damage is lipid peroxidation from lipoproteins, which leads to the generation of reactive carbonyl species that mediate macrophage recruitment, activation and proliferation. Also, the advanced lipoxidation end products formed by lipid peroxidation alter the structure and function of vascular walls[24].

However, not all studies have found such a positive relationship of total cholesterol and triglycerides with retinopathy; some have found no relationship[11–13],

one found high cholesterol to be protective of retinopathy[14] and yet another found an inverse association between cholesterol and the presence of retinopathy[24].

Rianita *et al*. felt that due to a majority of their patients having a normal lipid profile, the association was lacking with increasing severity of retinopathy[12]. Cetin *et al*. speculated that the association of retinopathy and lipids might be in the intraretinal lipid transport, and that serum lipids might be significantly associated only with advanced or severe stages of retinopathy[11]. Olivarius *et al*. studied only newly diagnosed diabetics and found an inverse association of triglycerides with retinopathy, but this finding was confined to patients with retinopathy having microalbuminuria[25].

We found a positive correlation of LDL with retinopathy, a finding similar to a couple of other studies[9,10]. Zhang *et al*. found, following adjustment for diabetes duration and systolic blood pressure by multivariate analysis, that hyperlipidemia, elevated VLDL and elevated triglycerides served as independent risk factors for the development and progression of retinopathy[26].

However, most studies found no association of LDL cholesterol with retinopathy[12,19,27]. Mathur *et al*. speculated that LDL elevation was found with overall lipid alteration among diabetics, but the significance was lost on comparison with diabetics having retinopathy while that with triglycerides was maintained[22].

HDL cholesterol was not significantly correlated with retinopathy in the current study, a finding that was consistent with most other studies[11–13,24]. Even though Sacks *et al*. found an association with HDL, after adjustment, this association was not found to be significant[28]. However, some studies found a link between reduced levels of HDL and increased prevalence of retinopathy[10,21,29]. The Wisconsin epidemiologic study of diabetic retinopathy found a protective effect of HDL in younger onset persons[30].

Hyperglycaemia is a known risk factor of retinopathy. Hyperglycaemia and dyslipidemia stimulate reactive oxygen species ROS production through protein kinase C PKC-dependent activation of nicotinamide adenine dinucleotide phosphate NADPH oxidase in endothelial cells leading to endothelial dysfunction[31].

Our study shows a strong positive correlation of fasting glucose with retinopathy. Other studies have also shown FBS to be associated with retinopathy[9,19,32–34]. Kim *et al*. found FBS to be an independent predictor of microvascular diabetic complications[35].

End products of glycosylation are indicative of endothelial dysfunction.[36] This endothelial dysfunction may contribute to microvascular changes leading to complications like retinopathy[37,38]. Elevated glycated end products, of which glycated haemoglobin is most commonly measured, are associated with poor glycaemic control and have been found to be associated with increased severity of microvascular complications compared to macrovascular diabetic complications[39]. Since retinopathy is also a common manifestation of microvascular complications of diabetes, it would stand to reason that glycated haemoglobin be associated with retinopathy. Our study shows a significant positive correlation of HbA1c with increasing severity of retinopathy. This was supported by other studies[7,29,40,41]. Increase in HbA1c significantly increased the risk for developing high risk proliferative diabetic retinopathy during a 5-year follow up[20]. The diabetes control and complications trial showed a significant role of HbA1c in the risk of progression of retinopathy in patients with insulin-dependent diabetes mellitus both in the conventional and intensive treatment groups[42]. HbA1c was found to be a significant risk factor for retinopathy after multiple logistic regression with an odds ratio of 1.21 per percent 14 and 1.26 per percent[43] increase in HbA1c.

However, all studies did not find a positive association between microvascular complications of diabetes and

glycated haemoglobin[44,45]. Biological variability in HbA1c values between individuals possibly restricts its predictive role with regards to diabetic complications[44].

Thus, there is a variation in the results of the studies attempting to correlate serum lipids and retinopathy. These variations do not seem to respect ethnic boundaries as seen in Indian studies[9,10,22,24] as well as European[8,25,43] or Chinese studies[26,34].

However, the positive correlation seen in this study and others do seem to justify a consideration for lipid lowering therapy, which has shown some effects in delaying progression to more severe forms of retinopathy[46].

CONCLUSION

Lipids have shown a positive correlation with the presence and severity of retinopathy. The laboratory parameters that correlate positively with increasing severity of retinopathy include: total cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol. These results suggest the study of lipid lowering therapies for possible benefit in patients with and without retinopathy.

REFERENCES

[1] Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD *et al*. Retinopathy in diabetes. Diabetes Care. 2004; 27 Suppl 1:s84–s87.

[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;467:2328–33.

[3] Nirmalan PK, Katz J, Robin AL, Tielsch JM, Namperumalsamy P, Kim R *et al*. Prevalence of vitreoretinal disorders in a rural population of southern India: The Aravind Comprehensive Eye Study. Arch Ophthalmol 2004;1224:581–86.

[4] Klein R, Klein BE, Moss SE, Linton KL. The beaver dam eye study: Retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus. Ophthalmology. 1992;991:58–62.

[5] Mitchell P, Smith W, Wang JJ, Attebo K. Prevalence of diabetic retinopathy in an older community: The Blue Mountains Eye Study. Ophthalmology 1998;1053:406–11.

[6] Klein R, Sharrett AR, Klein BEK, Moss SE, Folsom AR, Wong TY *et al*. The association of atherosclerosis, vascular risk factors, and retinopathy in adults with diabetes: The atherosclerosis risk in communities study. Ophthalmology 2002;1097:1225–34.

[7] Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy: III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol. 1984;1024:527–32.

[8] Van Leiden HA, Dekker JM, Moll AC, Nijpels G, Heine RJ, Bouter LM *et al*. Blood pressure, lipids, and obesity are associated with retinopathy: The Hoorn study. Diabetes Care. 2002;258:1320–5.

[9] Agroiya P, Philip R, Saran S, Gutch M, Tyagi R, Gupta KK. Association of serum lipids with diabetic retinopathy in type-2 diabetes. Indian J Endocrinol Metab. 2013 Oct; 17 Suppl 1:S335–337.

[10] Agrawal RP, Sharma P, Pal M, Kochar A, Kochar DK. Magnitude of dyslipedemia and its association with micro and macro vascular complications in type-2 diabetes: Ahospital based study from Bikaner Northwest India. Diabetes Res Clin Pract. 2006;732:211–14.

[11] Cetin EN, Bulgu Y, Ozdemir S, Topsakal S, Akin F, Aybek H *et al*. Association of serum lipid levels with diabetic retinopathy. Int J Ophthalmol. 2013;63:346–49.

[12] Rianita R, Bardosono S, Victor AA. Relationship between plasma lipid profile and the severity of diabetic retinopathy in type-2 diabetes patients. Med J Indones. 2008;221-5

[13] Benarous R, Sasongko MB, Qureshi S, Fenwick E, Dirani M, Wong TY *et al*. Differential association of serum lipids with diabetic retinopathy and diabetic macular edema. Invest Ophthalmol Vis Sci 2011 Sep 1;5210:7464–69.

[14] Wong TY, Cheung N, Tay WT, Wang JJ, Aung T, Saw SM *et al*. Prevalence and risk factors for diabetic retinopathy: The Singapore Malay eye study. Ophthalmology. 2008;11511:1869–75.

[15] Early treatment diabetic retinopathy Study design and baseline patient characteristics. ETDRS report number 7. Ophthalmology 1991;985 Suppl: 741–56.

[16] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;186:499–502.

[17] Goldberg IJ. Clinical review 124: Diabetic dyslipidaemia: Causes and consequences. J Clin Endocrinol Metab 2001;863:965–71.

[18] Kareem I, Jaweed SA, Bardapurkar JS, Patil VP. Study of magnesium, glycosylated haemoglobin and lipid profile in diabetic retinopathy. Indian J Clin Biochem. 2004;192:124–27.

[19] Rema M, Pradeepa R. Diabetic retinopathy: An Indian perspective. Indian J Med Res 2007;1253:297–310.

[20] Davis MD, Fisher MR, Gangnon RE, Barton F, Aiello LM, Chew EY *et al*. Risk factors for high-risk proliferative diabetic retinopathy and severe visual loss: Early treatment diabetic retinopathy study report #18. Invest Ophthalmol Vis Sci. 1998;392:233–52.

[21] Rahman MR, Arslan MI, Hoque MM, Mollah FH, Shermin S. Serum lipids and diabetic retinopathy in newly diagnosed type-2 diabetic subjects. J Enam Med Coll [Internet]. 2012 Jul 29 [cited 2014 Jun 10];12. Available from: http://www.banglajol.info/index.php/JEMC/article/view/11464

[22] Mathur A, Mathur R. Study of association of serum lipids with diabetic retinopathy in type-2 diabetes. Peoples J Sci Res. 2013;61:25–8.

[23] Landmesser U, Hornig B, Drexler H. Endothelial dysfunction in hypercholesterolemia: Mechanisms, pathophysiological importance, and therapeutic interventions. Semin Thromb Hemost. 2000;265:529–37.

[24] Vinodhini VM, Ganeswaran S, Ebenezer William W, Kumar JS, Jeevanathan A, Poonguzhali DV. A study on the pattern of lipid profile and apolipoproteins in patients with diabetic retinopathy. Int J Pharm Clin Res. 2013;51:1–3.

[25] De Fine ON, Nielsen NV, Andreasen AH. Diabetic retinopathy in newly diagnosed middle-aged and elderly diabetic patients. Prevalence and interrelationship with microalbuminuria and triglycerides. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Für Klin Exp Ophthalmol. 2001;2399:664–72.

[26] 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 B. 2013;145:392–99.

[27] Niskanen L, Uusitupa M, Sarlund H, Siitonen O, Voutilainen E, Penttilä I *et al*. Microalbuminuria predicts the development of serum lipoprotein abnormalities favouring atherogenesis in newly diagnosed type-2 non-insulin-dependent diabetic patients. Diabetologia. 1990;334:237–43.

[28] Sacks FM, Hermans MP, Fioretto P, Valensi P, Davis T, Horton E *et al*. Association between plasma triglycerides and high-density lipoprotein cholesterol and microvascular kidney disease and retinopathy in type 2 diabetes mellitus: Aglobal case-control study in 13 countries. Circulation. 2014;1299:999–1008.

[29] Longo-Mbenza B, Mvitu MM, Masamba W, Muizila KL, Longo PI, Kibokela ND *et al*. Retinopathy in non-diabetics, diabetic retinopathy and oxidative stress: Anew phenotype in Central Africa? Int J Ophthalmol 2014;72:293–301.

[30] Klein BE, Moss SE, Klein R, Surawicz TS. The Wisconsin epidemiologic study of diabetic retinopathy: XIII. Relationship of serum cholesterol to retinopathy and hard exudate. Ophthalmology 1991;988:1261–65.

[31] Inoguchi T, Li P, Umeda F, Yu HY, Kakimoto M, Imamura M*et al*. High glucose level and free fatty acid stimulate reactive oxygen species production through protein kinase C—dependent activation of NADPH oxidase in cultured vascular cells. Diabetes. 2000;4911:1939–45.

[32] Jayalakshmi V, Satya Narayana K, Sravanthi K, Ivvala AS. The evaluation of serum fasting blood sugar and lipid profile including Apo A and Apo B in diabetic retinopathy subjects. Indian J Basic Appl Med Res. 2012;12:94-102.

[33] Ballard DJ, Melton LJ 3rd, Dwyer MS, Trautmann JC, Chu CP, O'Fallon WM *et al*. Risk factors for diabetic retinopathy: Apopulation-based study in Rochester, Minnesota. Diabetes Care. 1986 Aug;94:334–42.

[34] Wang FH, Liang YB, Peng XY, Wang JJ, Zhang F, Wei WB *et al*. Risk factors for diabetic retinopathy in a rural Chinese population with type 2 diabetes: The Handan eye study. Acta Ophthalmol Copenh. 2011;894:e336–343.

[35] Kim JI, Stevens RJ, Holman RR. FPG and HbA1c are independent risk factors for microvascular but not macrovascular complications in newly diagnosed type-2 diabetes. Diabetologia 2005;48:A33

[36] Tan KCB, Chow W-S, Ai VHG, Metz C, Bucala R, Lam KSL. Advanced glycation end products and endothelial dysfunction in type-2 diabetes. Diabetes Care 2002;256:1055–59.

[37] Bandyopadhyay U, Das D, Banerjee RK. Reactive oxygen species: Oxidative damage and pathogenesis. Curr Sci. 1999;775:658–66.

[38] Guerci B, Böhme P, Kearney-Schwartz A, Zannad F, Drouin P. Endothelial dysfunction and type-2 diabetes: Part 2. altered endothelial function and the effects of treatments in type-2 diabetes mellitus. Diabetes Metab 2001;274 Pt 1:436–47.

[39] Sabanayagam C, Liew G, Tai ES, Shankar A, Lim SC, Subramaniam T *et al*. Relationship between glycated haemoglobin and microvascular complications: Is there a natural cut-off point for the diagnosis of diabetes? Diabetologia. 2009;527:1279–89.

[40] Nathan DM, Singer DE, Godine JE, Harrington CH, Perlmuter LC. Retinopathy in older type-II diabetics association with glucose control. Diabetes 1986;357:797–801.

[41] Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T *et al*. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care 2012;353:556–64.

[42] The relationship of glycaemic exposure HbA1c to the risk of development and progression of retinopathy in the diabetes control and complications trial. Diabetes 1995;448:968–83.

[43] Hove MN, Kristensen JK, Lauritzen T, Bek T. The prevalence of retinopathy in an unselected population of type-2 diabetes patients from Arhus County, Denmark. Acta Ophthalmol Scand. 2004;824:443–48.

[44] Jeffcoate SL. Diabetes control and complications: The role of glycated haemoglobin, 25 years on. Diabet Med J Br Diabet Assoc. 2004;217:657–65.

[45] Güven D, Ozdemir H, Hasanreisoglu B. Hemodynamic alterations in diabetic retinopathy. Ophthalmology 1996;1038:1245–49.

[46] Dodson PM. Management of diabetic retinopathy: Could lipid-lowering be a worthwhile treatment modality? Eye Lond Engl 2009;235:997–1003.

Received: 18.02.2015
Accepted: 06.05.2015