ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 6, Issue – 4, August – 2021 , Page No. : 117 - 122

Role of Dyslipidemia in diabetic retinopathy

[1]Dr Arun Mishra, Assistant Professor, Department of Biochemistry, Index Medical College Hospital And Research Center, Indore, MP

[2]Dr Sapneh Sharma, Department of Biochemistry, SOS, Jiwaji University, Gwalior, MP

Corresponding Author: Dr Arun Mishra, Assistant Professor, Department of Biochemistry, Index Medical College Hospital and Research Center, Indore, MP

Citation this Article: Dr Arun Mishra, Dr Sapneh Sharma, "Role of Dyslipidemia in diabetic retinopathy", IJMSIR- August - 2021, Vol – 6, Issue - 4, P. No. 117 – 122.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders characterized by hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics, environmental factors, and life-style choices. Depending on the etiology of the diabetes mellitus, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. Type 2 DM is due primarily to lifestyle factors and genetics (Ripsin CM *et al*., 2009). A number of lifestyle factors are known to be important to the development of type 2 DM. These are physical inactivity, sedentary lifestyle, cigarette smoking and generous consumption of alcohol (Hu FB et al., 2001). Obesity has been found to contribute to approximately 55% of cases of type 2 DM (CDC Report 2004). In India, Type 2 DM is the leading cause of end-stage renal disease (ESRD), non traumatic lower extremity amputations, and adult blindness. With increasing incidences in developing nations like ours, DM will be a leading cause of morbidity and mortality for the foreseeable future.

Diabetic retinopathy **(**DR) is a vascular complication of diabetes predominantly affecting the integrity of the microscopic vessels found in the retina. DR can be broadly divided into two stages: non proliferative (NPDR) and proliferative diabetic retinopathy (PDR). During non proliferative stage, the earliest visible sign of retinal damage results from abnormal permeability and/or non perfusion of capillaries, leading to the formation of micro aneurysms. Abnormal capillary permeability results in the leaking of fluid and solutes into the surrounding retinal tissue, which collects around the macula; this is referred to as macular edema (MO) and it threatens visual acuity. Proliferative stage develops following the occlusion of retinal capillaries leading to retinal ischemia, which promotes the development of neovascularization. The newly formed vessels are fragile so they hemorrhage easily. This results in accumulation of blood in the vitreous cavity impairing vision. This may be permanent due to further complications such as traction retinal detachment leading to complete blindness. Dyslipidemia is one of the major risk factors for both macro and micro vascular disease in diabetes mellitus. The characteristic features

of diabetic dyslipidemia are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased concentration of small dense LDL-cholesterol particles. The lipid changes associated with diabetes are attributed to increased free fatty acid flux secondary to insulin resistance. Proangiogenic marker vascular endothelial growth factor (VEGF), correlate with the presence and severity of DR (Kaul K *et al*., 2010) Activation of multiple cellular pathways, primarily mediated by hyperglycemia, are considered to play an important role in the pathogenesis of diabetic retinopathy. The metabolic effects of hyperglycemia result in micro vascular damage of the retina that leads to vascular leakage (non-proliferative diabetic retinopathy (NPDR)) and ischemia-induced retinal neovascularization (proliferative diabetic retinopathy (PDR)). These events lead to the up regulation of proangiogenic and inflammatory factors VEGF which has been extensively studied in the pathogenesis of DR, and new pharmacotherapies predominantly target the VEGF molecule, Furthermore, the use of anti-VEGF therapy in diabetic macular edema is not as robust as in retinal angiogenesis (PDR). Hyperglycemia induced diabetic retinopathy (DR) is an important micro vascular complication and is one of the leading cause of blindness in the working-age population of our country.

Material and methods

The study was carried out in the Department of Biochemistry, Mahatma Gandhi Memorial Medical College, Indore. The study included total of 240 subjects which were further divide into four groups containing 60 subjects each. **Group 1** or the control group included healthy subjects (n= 60), **group 2** included subjects who had diabetes but no sign of diabetic retinopathy (DWDR, n=60), **group 3** included subjects diagnosed with non proliferative diabetic retinopathy (NPDR, n=60), **group 4** included subjects with proliferative diabetic retinopathy (PDR, n=60).

Fasting blood glucose, visual acuity test and fundus dilated examination were the criteria for selection of DR patients. Patients were screened in the outpatient department and assigned in different groups. The serum sample obtained by processing the blood was analyzed for lipid profile and fasting blood glucose estimation using kit methods in auto analyzer (Bioline). Data regarding BMI, ag3, sex and duration of diabetes type 2 was also recorded. Statistical software, SPSS version 17.0 Trial was used for analysis of data. Overall, selected parametric values among studied samples was recorded, analyzed and compared to establish a relationship between hyperglycemia induced inflammation and irregular serum lipids.

Age

The older age group of 55-65 years comprised of 41.7% of group 1, 41.7% of group 2, 33.3 % of group 3 and 45.0% patients of group 4 respectively. The lower age group of 35-45 years comprised of fewer patients, only 8.3%, 15.0%, 8.3 and 0 samples belonged to group 1, group 2, group 3 and group 4 respectively (Table 1). The results clearly showed that age group 45-50 years had maximum numbers of patients with diabetes (T2DM) and diabetic retinopathy (DR) among all age groups, thus clearly enforcing that fact that chances of type 2 diabetes mellitus and retinopathy increases with increase in age.

Duration of diabetes

In our study we found that the major part of the population (75.0%) of patients of group 2 (DWDR) who didn't had retinopathy had 0-5 years of duration of diabetes. The duration of 5-10 years was observed more common among patients of group 4 (53.3%) with proliferative retinopathy (PDR) followed by less than

half (46.7%) patients of group 3 (NPDR) and exactly one-fourth (25.0%) patients of group 2(DWDR). Diabetes duration of 10-15 years was seen only among group 3 and group 4. Seventeen (28.3%) patients of group 4 had diabetes duration of 10-15 years followed by eight (13.3%) patients of group 3 with non proliferative diabetic retinopathy. Duration of ≥15 years was observed more common among 13.3% patients of group 4 with proliferative retinopathy followed by 1.7% of group 3 patients.

Table 1: Frequency and percentage distribution of age of subjects in groups

Age (year)	Group 1		Group 2		Group 3		Group 4	
	n1	%	n2	%	n3	%	n4	%
35-45	5	8.3	9	15.0	5	8.3	0	0.0
45-55	25	41.7	19	31.7	34	56.7	26	43.3
55-65	25	41.7	25	41.7	20	33.3	27	45.0
65-75	5	8.3	7	11.7	1	1.7	7	11.7
Total	60	100.0	60	100.0	60	100.0	60	100.0

Moreover, the mean duration of diabetes (Mean ± Standard Deviation) of patients of group 4 (PDR) was found to be significantly greater (9.72±3.96 year) as compared to patients of group 3(NPDR) (6.22±3.34 year) and patients of group 2 (DWDR) (3.78±1.54 year) and controls (0.0±0.00 year). However, the differences in mean diabetic retinopathy duration among groups were statistically highly significant ($p<0.001$).

Table 2: Assessment of duration of diabetes in subjects in four groups

Diabetic retinopathy duration	Group 1		Group 2		Group 3		Group 4	
	n1	%	n2	%	n3	%	n4	%
0-5 year	0	0.0	45	75.0	23	38.3	3	5.0
5-10 year	0	0.0	15	25.0	28	46.7	32	53.3
10-15 year	0	0.0	0	0.0	8	13.3	17	28.3
≥15 year	0	0.0	0	0.0	1	1.7	8	13.3
Mean ± Std. Deviation	0.0±0.00 year		3.78±1.54 year		6.22±3.34 Year		9.72±3.96 year	

The mean difference in duration is highly significant among four groups at the 0.001 level of significance ($p<0.001$).

In the study it was observed that the average (mean ± standard deviation) FBS of patients of diabetes mellitus with proliferative retinopathy (PDR) (192.43±30.72 mg/dl) was found to be significantly higher as compared with non-proliferative retinopathy (NPDR) (180.58±14.49 mg/dl)) and that followed by diabetes mellitus without retinopathy patients (166.65±21.12 mg/dl) and healthy controls (110.35±11.54 mg/dl). However, one way analysis of variance indicated that these differences in mean FBS among four groups were highly significant ($p<0.001$).

The WESDR XIII study there was a significant trend towards an association between increasing severity of diabetic retinopathy and of retinal hard exudate and increasing cholesterol in diabetic persons (Klein BE et al, 1991).

According to Hoorn study (2002) the patients who had elevated serum total cholesterol or elevated serum low-density lipoprotein cholesterol (LDL-C) were more likely to have retinal hard exudate. The prevalence of retinopathy was positively associated with elevated BMI, serum cholesterol and triglyceride levels in all glucose categories. In addition, elevated blood pressure and plasma total and LDL cholesterol levels showed associations with retinal hard exudate (Van Leiden HA *et al.*,2002).

In our study it was observed that the average (mean ± standard deviation) total cholesterol of diabetes mellitus with proliferative retinopathy patients (257.92±31.69 mg/dl) was found to be significantly larger as compared to diabetes mellitus without retinopathy patients (243.30±22.96 mg/dl) and that followed by diabetes mellitus patients with non-proliferative retinopathy (230.98±32.96 mg/dl)) and healthy controls (189.45±14.28 mg/dl) (Table 3). However, one way analysis of variance indicated that these differences in mean total cholesterol among four groups were highly significant ($p<0.001$) (Table 3).

Among diabetes mellitus with proliferative retinopathy patients, the mean triglyceride (259.77±51.61 mg/dl) was found to be significantly elevated as compared to diabetes mellitus with non-proliferative retinopathy patients (223.78±48.67 mg/dl) and followed by diabetes mellitus without retinopathy patients (211.02±45.68 mg/dl) and healthy control patients (181.37±20.88 mg/dl) (Table 3). However, one way analysis of variance indicated that these differences in mean Triglyceride among four groups were highly significant ($p<0.001$) (Table 3). Average LDL of diabetes mellitus with proliferative retinopathy patients (171.43±30.24 mg/dl) was found to be significant increased as compared to diabetes mellitus without retinopathy patients (156.20±20.65 mg/dl) and that followed by diabetes mellitus with non-proliferative retinopathy patients (145.47±31.31 mg/dl) and healthy controls (104.80±17.02 mg/dl) (Table 3).

Overall, one way analysis of variance indicated that these differences in mean LDL among four groups were highly significant ($p<0.001$) (Table 3). The mean (34.15±6.03 mg/dl) HDL of diabetes mellitus with proliferative retinopathy patients was found to be significantly minimum as compared to diabetes mellitus without retinopathy patients (44.96±8.82 mg/dl) and that followed by diabetes mellitus with non- proliferative retinopathy patients (41.27±5.37 mg/dl) and healthy controls (48.00±10.41 mg/dl) (Table 3). Overall, one way analysis of variance indicated that these differences in mean HDL among four groups were highly significant ($p<0.001$) (Table 3).

The average VLDL (52.24±10.62 mg/dl) levels of diabetes mellitus with proliferative retinopathy patients was significantly elevated as compared to diabetes mellitus with non-proliferative retinopathy patients (44.83±9.78 mg/dl) and followed by diabetes mellitus without retinopathy patients (42.12±9.02 mg/dl) and healthy control patients (36.49±4.25 mg/dl) (Table 3). However, one way analysis of variance indicated that these differences in mean VLDL among four groups were highly significant ($p<0.001$) (Table 3).

Table 3: Comparison of cholesterol, triglyceride, LDL, HDL and VLDL of controls and patients

Variable	Group	Spread	95% Confidence Intervals of Mean		p-value (LOS)
		Mean ± SD	LB	UB	
Cholesterol (mg/dl)	Group 1	189.45±14.28	185.76	193.14	F=73.73
	Group 2	243.30±22.96	237.37	249.23	p<0.001 #
	Group 3	230.98±32.96	222.47	239.50	
	Group 4	257.92±31.69	249.73	266.10	
Triglyceride (mg/dl)	Group 1	181.37±20.88	175.97	186.76	F=33.51
	Group 2	211.02±45.68	199.22	222.82	p<0.001 #
	Group 3	223.78±48.67	211.21	236.36	
	Group 4	259.77±51.61	246.43	273.10	
LDL (mg/dl)	Group 1	104.80±17.02	100.41	109.20	F=74.73
	Group 2	156.20±20.65	150.87	161.54	p<0.001 #
	Group 3	145.47±31.31	137.38	153.56	
	Group 4	171.43±30.24	163.62	179.25	
HDL(mg/dl)	Group 1	48.00±10.41	45.31	50.68	F=34.04
	Group 2	44.96±8.82	42.69	47.24	p<0.001 #
	Group 3	41.27±5.37	39.88	42.66	
	Group 4	34.15±6.03	32.59	35.70	
VLDL(mg/dl)	Group 1	36.49±4.25	35.39	37.59	F=33.40
	Group 2	42.12±9.02	39.79	44.45	p<0.001 #
	Group 3	44.83±9.78	42.30	47.35	
	Group 4	52.24±10.62	49.50	54.98	

Discussion

Impaired glucose metabolism, lipid abnormalities, vascular dysfunction and inflammation are the key components of the diabetic retinopathy.

Duration of diabetes is an important factor in the development of its complications. The incidence of DR increases with diabetes duration, increasing linearly after 10 years, and it is detected in one-third of all patients with DM for 25 years (Hietala K et al, 2010). In our study we found that the major part of the population (75.0%) of patients of group 2 (DWDR) who didn't had retinopathy had 0-5 years of duration of diabetes.

Statistical analysis of our study has projected that total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein of diabetic patients with proliferative retinopathy found to be significantly elevated but high density lipoprotein was significantly decreased as compared to patients of diabetes mellitus with and without retinopathy and healthy controls.

There is a significant trend towards an association between increasing severity of diabetic retinopathy and of retinal hard exudate and increasing cholesterol in diabetic persons (Klein BE et al, 1991). Statistical analysis of our study has projected that total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein of diabetic patients with proliferative retinopathy found to be significantly elevated but high density lipoprotein was significantly decreased as compared to patients of diabetes mellitus with and without retinopathy and healthy controls.

Conclusions

As the duration of diabetes increases risk of advanced stage of retinopathy also increases. The present study

reinforces the role of irregular lipid levels in serum to diabetic retinopathy and the association of hyperglycemia and dyslipidemia.

References

1. Antonetti DA, Barber AJ, Hollinger LA, Wolpert EB, Gardner TW. Vascular endothelial growth factor induces rapid phosphorylation of tight junction proteins occludin and zonula occluden 1. A potential mechanism for vascular permeability in diabetic retinopathy and tumors. J Biol Chem. 1999;274(33):23463–7.
2. Cavusoglu AC, Bilgili S, Alaluf A, Doğan A, Yilmaz F, Aslanca D, Karaca B, Yüksel B, Topaloglu E. Vascular endothelial growth factor level in the serum of diabetic patients with retinopathy. Ann Ophthalmol (Skokie) 2007;39:205–8.
3. Doganay S, Evereklioglu C, Er H, Türköz Y, Sevinç A, Mehmet N, et al. Comparison of serum NO, TNF-alpha, IL-1beta, sIL-2R, IL-6 and IL-8 levels with grades of retinopathy in patients with diabetes mellitus. Eye. 2002;16:163–70.
4. Hietala K, Harjutsalo V, Forsblom C, Summanen P, Groop PH FinnDiane Study Group. Age at onset and the risk of proliferativ retinopathyintype 1 diabetes. Diabetes Care. 2010;33:1315–1319.
5. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitusin women. N Engl J Med. 2001;345:790–797.
6. Kaul K, Hodgkinson A, Tarr JM, Kohner EM, Chibber R. Is inflammation a common retinal-renal-nerve pathogenic link in diabetes? Curr Diabetes Rev. 2010;6:294–303.
7. Klein BE, Knudtson MD, Tsai MY, Klein R. The relation of markers of inflammation and endothelial dysfunction to the prevalence and progression of diabetic retinopathy: Wisconsin epidemiologic study of diabetic retinopathy. Arch Ophthalmol. 2009;127:1175–82.
8. 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;98(8):1261–1265.
9. Petrovic MG, Korosec P, Kosnik M, Osredkar J, Hawlina M, Peterlin B, Petrovic D. Local and Genetic Determinants of Vascular Endothelial Growth Factor Expression in Advanced Proliferative Diabetic Retinopathy. Mol Vis. 2008;14:1382–7.
10. Ripsin CM, Kang H, Urban RJ. Management of blood glucose in type 2 diabetes mellitus. Am Fam Physician 2009 Jan;79(1):29-36.