Correlation of serum lipids with the severity of diabetic retinopathy

Nada Nadeem Ansari[1], Abdul Waris[2,*], Adeeb Alam Khan[3], Sheelu Shafiq Siddiqi[4]

[1]Junior Resident, [2]Assistant Professor, [3]Professor, [4]Associate Professor, [1-3]Dept. of Ophthalmology, [4]Dept. of Medicine, Jawaharlal Nehru Medical College Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

***Corresponding Author:**
Email: waris_eye@yahoo.co.in

Abstract

Purpose: To measure a correlation between serum lipids and the severity of diabetic retinopathy in patients reporting to a tertiary care diabetic and endocrinology center, in western Uttar Pradesh.

Method: A hospital-based, cross-sectional study conducted on 240 eyes of 120 diabetic patients presenting at our Institute of Ophthalmology. The ETDRS system was used to grade the severity of retinopathy and the serum lipid profile of each patient was procured. The data analysis was done with the help of SPSS version 16.0 using unpaired t-test, binary logistic regression analysis, one way analysis of variance (ANOVA) with Bonferroni post hoc tests.

Result: A significantly increased level of total cholesterol (p=0.02), TG (p=0.0001) and LDL (p=0.0001) was found among patients with DR than without DR. The total cholesterol was found to be significantly ($p<0.05$) lower among the patients with mild NPDR than mild-moderate PDR, and high risk PDR. The TG level was significantly ($p<0.05$) different among various stages of retinopathy. The HDL was significantly ($p<0.05$) higher among the patients with mild NPDR than mild-moderate PDR. Similarly, the LDL level was significantly ($p<0.05$) lower among the patients with mild NPDR than mild-moderate PDR.

Conclusion: An increased level of total cholesterol, TG and LDL was found among patients with DR than without DR. The levels of total cholesterol, TG and LDL were found to be significantly lower among the patients with mild NPDR than PDR. The HDL level was higher among the patients with mild NPDR than mild-moderate PDR.

Keywords: Diabetic retinopathy, HDL, LDL, Lipids, TG.

Introduction

Diabetes Mellitus (DM) and the eye diseases associated with it comprise a set of complex disorder with multi-factorial etiology, where both genetic and environmental factors play an active role. It is a major cause of avoidable blindness in both the developed and developing countries. Newly diagnosed diabetic cases are increasing at an alarming rate in the developing countries like India due to better life style and urbanization with improved access to the health care system. Approximately, 382 million people across the world have been estimated to have DM in 2013 and if no action is taken this number will rise to 592 million by 2035.(1) WHO estimates that 19% of the world's diabetic population lives in India and 80 million people in India will have diabetes by the year 2030.(2) Diabetic retinopathy (DR) is the most common complication of diabetes mellitus. An early diagnosis with the help of better screening and referral facilities, strict control of systemic parameters and timely management in the form of medical and surgical intervention can delay the sight threatening complications of DR.

Materials and Methods

This hospital based cross-sectional study was conducted after getting an approval from the Ethical Committee, Jawaharlal Nehru Medical College and Hospital, A.M.U., Aligarh, and was according to the Declaration of Helsinki. An informed written consent was taken from each patient before their participation in the study.

Inclusion Criteria: All 240 eyes of 120 patients with age greater than 20 years, and having a reasonably clear media which were referred to the Retina Clinic, Institute of Ophthalmology, Jawaharlal Nehru Medical College and Hospital, A.M.U., Aligarh from January 2016 to October 2017, after being referred from Rajiv Gandhi Center for Diabetes and Endocrinology, of the same hospital.

Exclusion Criteria:

1. The patients with media not clear.
2. The patients with gestational diabetes mellitus.
3. The patients where fundus photography was not possible (in any particular eye or field) due to inadequate dilatation or an inability to co-operate, properly.

A clinical history was taken with the help of a structured questionnaire including- demographic data, duration of diabetes, treatment taken, addiction, dietary habits, family history of diabetes, and blood pressure. The laboratory profile consisted of serum lipids (normal values: LDL<70mg/dL, total cholesterol<200mg/dL, HDL<40mg/dl (low) and >=6omg/dl (high)).

A thorough clinical examination was done to grade the severity of diabetic retinopathy appropriately with the help of dilated fundus examination using Slit Lamp Biomicroscopy, Direct Ophthalmoscopy, Indirect Ophthalmoscopy, Fundus Fluorescein Angiography and OCT. A fundus photograph using Visucam 500 was taken and the modified Airlie House classification of diabetic retinopathy was used in the present study to grade the severity of diabetic retinopathy in diabetic patients, who reported at our center.

The data collected was analysed for statistical significance using SPSS version 16.0 version (Chicago, Inc., USA). The binary logistic regression analysis was carried out to find the strength of association between severity of DR and serum lipids. The odds ratio (OR) with its 95 per cent confidence interval was calculated. Unpaired t-test was used to compare the continuous variables between two strata. The one way analysis of variance (ANOVA) with Bonferroni post hoc tests were used to compare more than two means. The p-value<0.05 was considered significant.

Observation and Results

The overall prevalence of DR was found to be 52.5%, out of 120 diabetic patients who were included in the study.

Table 1: Comparison of lipid profile between patients with DR and without DR

Lipid profile	With DR	Without DR	p-value[1]
Cholesterol	227.49±92.83	188.91±88.02	0.02*
TG	194.95±74.00	147.98±48.98	0.0001*
HDL	45.46±15.42	46.63±12.46	0.65
LDL	128.06±43.43	97.75±39.09	0.0001*

[1]Unpaired t-test, *Significant

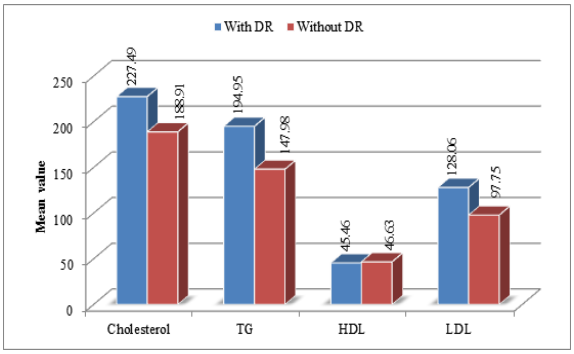

Fig. 1: Comparison of lipid profile between patients with DR and without DR

A significantly increased level of total cholesterol (p=0.02), TG (p=0.0001) and LDL (p=0.0001) was found among patients with DR than without DR. However, insignificantly (p>0.05) decreased level of HDL was found among patients with DR than without DR. (Table 1, Fig. 1)

Table 2: Comparison of total cholesterol with stage of retinopathy

Stage of retinopathy	Total cholesterol (mg/dL)	
	Right eye	Left eye
Mild NPDR	194.80±27.02[a,b]	195.50±29.63[a,b]
Moderate NPDR	235.50±72.48	233.00±72.09
Severe NPDR	289.75±101.33	303.40±95.01 [a]
Mild-moderate PDR	332.71±127.19 [a]	330.75±113.76[b]
High-risk PDR	345.75±155.80 [b]	279.00±138.36
ADED	225.00±74.23	228.67±90.47
p-value[1]	0.0001*	0.0001*

[1]ANOVA test, *Significant, [a,b]p<0.05 (Post hoc tests)

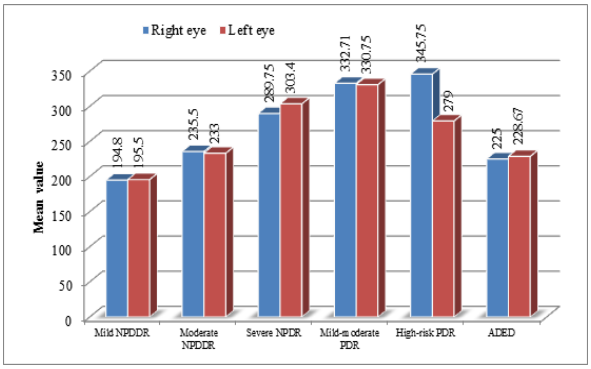

Fig. 2: Comparison of total cholesterol with stage of retinopathy

The analysis of variance showed that there was a significant difference in total cholesterol among stages of retinopathy in both right and left eye groups (p=0.0001). The post-hoc tests revealed that total cholesterol was significantly (p<0.05) lower among the patients with mild NPDR (194.80±27.02 mg/dL) than mild-moderate PDR (332.71±127.19mg/dL), and high risk PDR (345.75±155.80 mg/dL) in right eye group. The total cholesterol was also observed to be significantly (p<0.05) lower among the patients with mild NPDR (195.50±29.63 mg/dL) than mild-moderate PDR (330.75±113.76 mg/dL) in left eye group. (Table 2, Fig. 2)

Table 3: Comparison of serum triglycerides (TG) with stage of retinopathy

Stage of retinopathy	TG (mg/dL)	
	Right eye	Left eye
Mild NPDR	148.67±31.18 [a]	154.75±35.58 [a]
Moderate NPDR	214.50±77.53 [a]	192.70±55.32 [a]
Severe NPDR	256.00±71.91 [a]	292.00±71.90 [a]
Mild-moderate PDR	278.86±51.89 [a]	280.00±46.80 [a]
High-risk PDR	259.50±49.27 [a]	249.83±36.42 [a]
ADED	248.75±51.36 [a]	246.33±62.63 [a]
p-value[1]	0.0001*	0.0001*

[1]ANOVA test, *Significant, [a]p<0.05 (Post hoc tests)

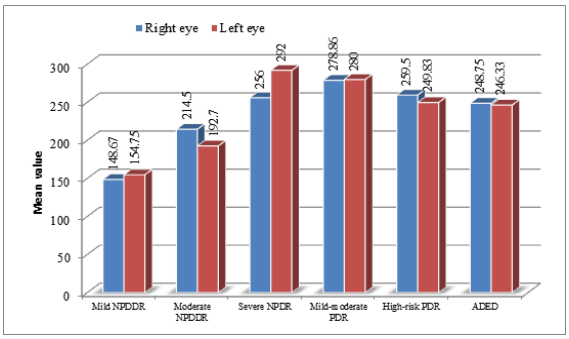

Fig. 3: Comparison of TG with stage of retinopathy

The analysis of variance showed that there was a significant difference in TG among stages of retinopathy in both right and left eye (p=0.0001). The post-hoc tests revealed that TG was significantly (p<0.05) different among the various stages of retinopathy in both right and left eye groups. (Table 3, Fig. 3)

Table-4: Comparison of HDL with stage of retinopathy

Stage of retinopathy	HDL (mg/dL)	
	Right eye	Left eye
Mild NPDR	55.33±14.33 [a]	53.00±11.56[a,b]
Moderate NPDR	43.40±16.57	45.40±15.14
Severe NPDR	35.75±8.85	32.60±7.23 [a]
Mild-moderate PDR	32.43±5.86 [a]	33.00±5.88[b]
High-risk PDR	35.75±5.44	35.50±5.32
ADED	32.75±1.26	32.33±1.15
p-value[1]	0.001*	0.0001*

[1]ANOVA test, *Significant, [a,b]p<0.05 (Post hoc tests)

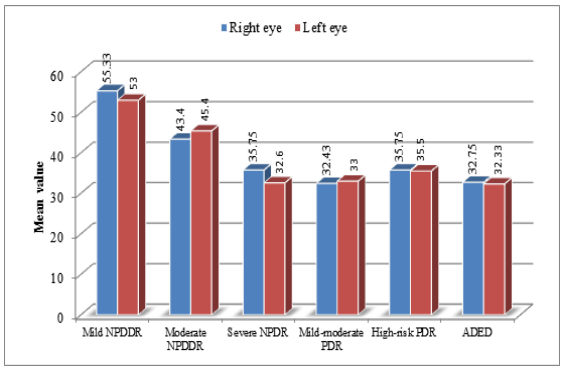

Fig. 4: Comparison of HDL with stage of retinopathy

The analysis of variance showed that there was a significant difference in HDL among stages of retinopathy in both right (p=0.001) and left eye groups (p=0.0001). The post-hoc tests revealed that HDL was significantly (p<0.05) higher among the patients with mild NPDR (55.33±14.33 mg/dL) than mild-moderate PDR (32.43±5.86 mg/dL) in right eye group. HDL was also found to be significantly (p<0.05) higher among the patients with mild NPDR (53.00±11.56 mg/dL) than mild-moderate PDR (33.00±5.88 mg/dL) in left eye group. (Table 4, Fig. 4)

Table-5: Comparison of LDL with stage of retinopathy

Stage of retinopathy	LDL (mg/dL)	
	Right eye	Left eye
Mild NPDR	102.67±27.49[a]	113.83±25.56[a,b]
Moderate NPDR	142.20±39.29	137.30±36.25
Severe NPDR	160.00±38.96	174.20±23.78 [a]
Mild-moderate PDR	168.14±43.18 [a]	179.88±42.17[b]
High-risk PDR	165.00±45.09	135.83±40.11
ADED	111.75±32.51	119.33±35.22
p-value[1]	0.001*	0.0001*

[1]ANOVA test, *Significant, [a,b]p<0.05 (Post hoc tests)

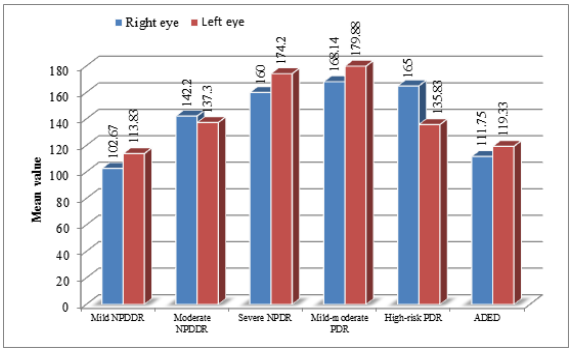

Fig. 5: Comparison of LDL with stage of retinopathy

The analysis of variance showed that there was a significant difference in LDL among stages of retinopathy in both right (p=0.001) and left eye (p=0.0001) groups. The post-hoc tests revealed that LDL was significantly (p<0.05) lower among the patients with mild NPDR (102.67±27.49 mg/dL) than mild-moderate PDR (168.14±43.18 mg/dL) in right eye group. LDL was also observed to be significantly (p<0.05) lower among the patients with mild NPDR (113.83±25.56 mg/dL) than mild-moderate PDR (179.88±42.17 mg/dL) in left eye group. (Table 5, Fig. 5)

Discussion

On analyzing the lipid profile, the levels of total cholesterol, triglycerides, and LDL were found to be significantly higher (p<0.05) in patients with DR than in those without DR. And also, there was a significant increment in their values with increasing severity of diabetic retinopathy. An insignificant decrease in the

level of HDL was noted among patients with DR than without DR. But there existed a significant decrement in HDL levels with increasing severity of diabetic retinopathy. The HDL level was significantly ($p<0.05$) higher among the patients with mild NPDR (55.33±14.33 mg/dL) than mild-moderate PDR (32.43±5.86 mg/dL) in right eye group. Similarly, in the left eye group, HDL level was found to be significantly ($p<0.05$) higher among the patients with mild NPDR (53.00±11.56 mg/dL) than mild-moderate PDR (33.00±5.88 mg/dL). This further highlights the importance of tight metabolic control for the prevention and progression of diabetic retinopathy.

High lipid levels are known to cause endothelial dysfunction due to a reduced bioavailability of nitric oxide and dysfunction of the vascular endothelium is regarded as an important factor in the pathogenesis of diabetic vascular complications.[3] Consequently, it was proposed that, hyperlipidemia might contribute to DR and Macular Edema (ME) by endothelial dysfunction and breakdown of the blood retinal barrier leading to exudation of serum lipids and lipoproteins.[4]

A poor lipid control hastens the progression of NPDR to PDR, and its related complications. The Wisconsin Epidemiologic Study of DR XIII study,[5] and ETDRS, have shown that total cholesterol (TC) and serum low-density lipoprotein cholesterol (LDL-C) are associated with the presence of hard exudates in patients with DR. The association between dyslipidemia and DR has also been studied in the CURES Eye Study,[6] which showed that TC, non high-density lipoprotein cholesterol (HDL-C) and serum triglycerides (TGs) were associated with DR.

Similar to our study, Mathur et al. also found that triglyceride levels were significantly raised ($p<0.05$) in subjects with diabetic retinopathy as compared to those without diabetic retinopathy but they did not find any association between low density lipoprotein and total cholesterol levels with the prevalence of diabetic retinopathy.[7]

The development of DR was positively correlated with the LDL level and negatively correlated with the HDL level, according to Agroiya et al.[8] In ETDRS it was shown that patients with high total cholesterol and LDL levels were more likely to have retinal hard exudates compared to patients with normal lipid profile.[9]

Another study conducted by Klein et al. revealed a modest association between higher levels of high-density lipoprotein cholesterol and decreased prevalence of proliferative diabetic retinopathy. But they did not find any association between serum total or high-density lipoprotein cholesterol and incident proliferative diabetic retinopathy or macular edema.[10]

Other studies showed that retinal exudates or ME was associated either with LDL or total cholesterol, or both.[11-14] Unlike the present study, Hove et al.[15] reported no significant association between DR, triglycerides, HDL and total cholesterol in diabetic population in Denmark.

Conclusion

1. An increased level of total cholesterol, TG and LDL was found among patients with DR than without DR.
2. The level of total cholesterol was found to be lower among the patients with mild NPDR than mild-moderate PDR and high risk PDR.
3. A progressive increase in triglyceride (TG) level occurred with increasing grade of diabetic retinopathy.
4. The level of HDL was higher among the patients with mild NPDR than mild-moderate PDR.
5. The LDL level was lower among the patients with mild NPDR than mild-moderate PDR.

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