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The Role of Lipid Profile and Glycosylated Haemoglobin on Fundus Changes in Diabetic Patients

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Abstract **Original Research Article**

Introduction*:** Elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy. Although retinal hard exudates usually accompany diabetic macular edema, increasing amounts of exudate appear to be independently associated with an increased risk of visual impairment. ***Objective: To evaluate the role of lipid profile and glycosylated haemoglobin on fundus changes in diabetic patients. ***Materials and methods*:** This is a cross sectional study conducted in Department of Ophthalmology Out patients and in patients of tertiary care teaching hospital. Patients were enrolled for the study after obtaining written informed consent. Total 214 patients were screened in this study. Collected data was analysed by both descriptive and inferential methods. ***Result:*** Majority of patients were in age group of 40-60 years with mean age 54.47 ± 12.24 years. Statistically significant correlation was found with increasing age and incidence of diabetic retinopathy (p=0.016). The prevalence of DR shown male predominance with male to female ratio was 2.6:1. Significant correlation was observed between triglyceride (p=0.007), total cholesterol(p=0.002) and LDL(p=0.149) levels with diabetic retinopathy. A positive correlation was observed between glycosylated haemoglobin (p<0.001) and severity of diabetic retinopathy**.** ***Conclusion:*** In our study a statistically significant correlation was obtained between severity of diabetic retinopathy with serum total cholesterol, triglycerides and LDL and glycosylated haemoglobin.

Keywords: Hyperlipidemia, Retinopathy, Modified Arlie House classification.

INTRODUCTION

Elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy. Although retinal hard exudates usually accompany diabetic macular edema, increasing amounts of exudate appear to be independently associated with an increased risk of visual impairment [1]. The elevated lipid levels are also associated with endothelial dysfunction which appears to play an important role in the pathogenesis of diabetic retinopathy, particularly in relation to the breakdown of blood retinal barrier.

Dyslipidemia and lipid peroxidation may play a role in pathogenesis of diabetic retinopathy. The control of lipid alteration through glycaemic control and/or lipid lowering medication is required for type 2 diabetic at least to postpone or prevent loss of vision from retinopathy [2].

Several tests have shown that serum and plasma total cholesterol concentrations have been strongly and positively associated with coronal artery atherosclerosis, spreading through a broad spectrum of total cholesterol levels and LDL cholesterol [3]. Dyslipidemia itself is considered to be a retinopathy and other ocular abnormality risk factor [4].

Various ocular manifestations, spectrum of findings and their association with components of lipid profile (LDL, HDL, VLDL, Total Cholesterol, and Triglycerides) may be helpful in risk stratification and in tailoring of lipid lowering treatment. In view of this, the current study aimed to evaluate the role of dyslipidemia on fundus changes in patients, and to correlate above findings with the components of lipid profile (LDL, HDL, VLDL, Total cholesterol and triglycerides) [5].

The present study is undertaken to determine the various fundus changes in diabetes mellitus in

association of serum lipid profile and elevated levels of HbA1C in absence of any renal abnormalities. The conflicting reports if any in the literature regarding the association and paucity of studies relative to the existing case load warrants this study.

OBJECTIVE

To evaluate the role of lipid profile and glycosylated haemoglobin on fundus changes in diabetic patients.

MATERIALS AND METHODS

This is a cross sectional study conducted in Department of Ophthalmology Out patients and in patients of tertiary care teaching hospital. Patients were enrolled for the study after obtaining written informed consent. Total 214 patients were screened in this study.

Methods: After obtaining a written informed consent patients were evaluated as follows:

1) Detailed diabetic status of the patient

- Age of onset
- Duration of the disease
- Associated conditions like hypertension, renal, cardiovascular, cerebrovascular disease
- Any medications (Hypoglycemic drugs, Lipid lowering drugs)
- Family history
- Other risk factors like smoking, alcohol, tobacco use were recorded.

2) Detailed ophthalmic examination

- Best corrected visual acuity
- Refraction
- Slit lamp examination of Anterior Segment
- Dilated fundus evaluation with
- Direct ophthalmoscope
- Indirect ophthalmoscope
- Slit lamp bio microscopy using 90D or 78D lens
- Findings were recorded in Amsler chart

Staging of Diabetic Retinopathy was done using Modified Arlie House classification.[13]

Inclusion criteria

1. Consented individual
2. OPD patients
3. In-Patients
4. Patients diagnosed to have diabetes mellitus.

Exclusion criteria

1. Patients with high myopia were excluded from the study.
2. Patients with hazy ocular media in both the eyes and other retinal vascular disorders were excluded from the study.

STATISTICAL ANALYSIS

Collected data was analysed by both descriptive and inferential methods. Descriptive methods such as mean and standard deviation were calculated for quantitative data, frequency and percentage were found out for categorical data.

Inferential methods such as chi square test was calculated to obtain the significance between the two parameters. ‘t’ test was used to compare various quantitative parameters between two categories.

ANOVA test and post hoc analysis was performed to obtain the significance across more than two categories.

SPSS analysis was performed using SPSS software 13 and ‘p’ value <0.05 is considered as significant.

RESULT

Table-1: AGE DISTRUBUTION

Age group in years	Frequency	Percentage (%)
<30	6	2.8
30-40	24	11.2
40 -50	39	18.2
50 -60	72	33.6
60 –70	52	24.3
70- 80	21	9.8
Total	214	100.0

The above table gives the age distribution across the 214 subjects. There were only 2.8% subjects who were below 30 years of age. 11.2% between 31-40 years of age, 18.2% subjects were between 41 and 50 years of age, 33.6% subjects were between 51-60 years of age, 24.3% subjects were between 61-70 years of age and 9.8% subjects were above 70 years of age. The mean age of the group was 54.47±12.24.

Table-2: Diabetic Retinopathy with gender distribution

		Sex		Total
		Male	Female	
No evidence	Number of subjects	37	17	54
	Percentage	26.8%	22.4%	25.2%
Mild	Number of subjects	48	33	81
	Percentage	34.8%	43.4%	37.9%
Moderate	Number of subjects	38	20	58
	Percentage	27.5%	26.3%	27.1%
Severe	Number of subjects	15	6	21
	Percentage	10.9%	7.9%	9.8%
Total	Number of subjects	138	76	214
	Percentage	64.4%	35.6%	100.0%

Among the total number of diabetic retinopathy patients, 138(64.5%) were males and 76(35.5%) were females. Out of total number of females in the study 77.6% had diabetic retinopathy and severity of diabetic retinopathy is more in males (10.9% versus 7.9%).There was no statistical significance with gender and diabetic retinopathy.

Table-3: Comparison of Total Cholesterol with Severity of Retinopathy

		N	Mean (mg/dl)	Std. Deviation	F	P
	No evidence	54	163.367	39.608		
	Mild	81	191.222	53.018		
	Moderate	58	190.603	53.321		
	Severe	21	203.000	50.697	4.97	0.002HS

Total Cholesterol level increases with severity of disease. With no Retinopathy mean total cholesterol was found to be 163.37mg/dl. But those who had severe retinopathy it was 211.944mg/dl and the difference among the different levels of retinopathy with Total cholesterol was found to be statistically significant.

Table-4: Comparison of Mean HDL with severity of Retinopathy.

		N	Mean (mg/dl)	Std. Deviation	H	P
HDL	No evidence	54	38.63	15.08		
	Mild	81	43.02	13.14		
	Moderate	58	40.81	21.00		
	Severe	18	44.06	17.86		
	Very severe	3	28.33	11.15	9.81	.044 sig

Mean HDL level progressively decreased from mild to very severe Retinopathy from 43.02mg/dl to 28.33mg/dl respectively and the difference was found to be statistically significant(p=0044).

Table-5: Comparison of Mean LDL according to severity Retinopathy

		N	Mean	Std. Deviation	H	P
LDL	No evidence	54	96.50	32.12		
	Mild	81	108.84	38.46		
	Moderate	58	115.15	41.10		
	Severe	18	111.79	42.40		
	Very severe	3	103.40	11.39	6.76	.149 ns

Comparison of mean LDL with grades of Retinopathy by using ANOVA. It was found, that mean LDL level was 108.5mg/dl and 111.79mg/dl in mild retinopathy and severe retinopathy respectively. The above difference was found to be statistically significant.

Table-6: Comparison of Triglyceride with the severity of Retinopathy

		N	Mean	Std. Deviation	H	P
TGL	No evidence	54	138.76	71.81		
	Mild	81	190.42	121.56		
	Moderate	58	171.53	78.89		
	Severe	18	181.83	74.69		
	Very severe	3	100.00	36.37	13.992	0.007 vhs

The mean Triglyceride level increases with no evidence of DR to severe DR from 138.76 mg/dl to 181.83mg/dl respectively. The above difference was statistically significant (p=0.007).

Table-7: Comparison of Mean FBS & PPBS according to Retinopathy

		N	Mean	Std. Deviation	F	P
FBS	No evidence	54	179.889	80.844		
	Mild	81	176.519	90.017		
	Moderate	58	181.793	79.237		
	Severe	18	205.056	89.417		
	Very severe	3	256.000	135.011	.982	.418ns
PPBS	No evidence	54	212.759	94.315		
	Very severe	3	266.33	112.3		

As the severity of DR increases, levels of both FBS & PPBS increases. When there was no evidence of Retinopathy the mean FBS & PPBS were 176.89 & 212.76mg/dl respectively. In very severe DR these values increase to 256 and 266.33 respectively. The difference was found to be statistically significant (p<0.001).

Table-8: Comparison of HbA1c level with severity of Retinopathy.

		N	Mean	Std. Deviation	H	P
Hba1c	No evidence	54	7.525	1.490		
	Mild	81	8.364	2.093		
	Moderate	58	8.605	1.657		
	Severe	18	10.026	1.985		
	Very severe	3	11.333	.551	45.994	<.001 vhs

Mean HbA1c levels increases with severity of DR changes. When there was no retinopathy the Mean HbA1c level was less than 7.525. The mean HbA1c levels increases from 8.364 to 11.333 in mild changes to severe changes of DR respectively. The above difference was found statistically significant(p<0.001)

DISCUSSION

High serum lipid levels are a risk factor for DR [6]. Dysfunction of the vascular endothelium is regarded as an important factor in the pathogenesis of diabetic vascular complications and has been shown to originate from dyslipidemia and hyperglycemia. Endothelial dysfunction in dyslipidemia is a result of multiple factors, including increased inactivation of nitric oxide by free radicals and inhibition of nitric oxide formation by different mechanisms. It was also reported that the lipid peroxidation in the vascular wall to local production of reactive carbonyl species that mediate recruitment of macrophages, cellular activation and proliferation and also chemical modification of vascular proteins by advanced lipoxidation end-products which affect both the structure and function of the vascular wall. Consequently, it was proposed that, hyperlipidemia might contribute to DR and ME by endothelial dysfunction and breakdown of the blood retinal barrier leading to exudation of serum lipids and lipoproteins. Hyperglycemia and its biochemical sequelae either directly or indirectly alter endothelial function by affecting the pathways of growth factors, cytokines and vasoactive agents.

The age and gender distribution were fairly consistent with findings of other related studies [7]. It was found that majority of patients were in age group of 40-60 years with mean age 54.47 ± 12.24 years. Statistically significant correlation was found with increasing age and incidence of diabetic retinopathy (p=0.016). The relationship of retinopathy was in concordance to that found in other studies. APED study [8], CURES Eye Study [9], Dondana *et al*. [10] have also found significant correlation between the age and diabetic retinopathy.

In the current study 76 were females and 138 were males, which corresponds to 35.5% and 64.5% respectively, out of which 27.6% of females and 72.4% of the males had diabetic retinopathy. The prevalence of

DR shown male predominance with male to female ratio was 2.6:1. In a clinical cohort of Chennai diabetic retinopathy appeared to be more prevalent in the males compared to females (sex ratio 2:1) [11]. Similar preponderance was seen in the CURES Eye study [12] and UKPDS study. However, the difference was not statistical significance with respect to the sex distribution in this study (p=0.529).

Total cholesterol level increases with severity of DR. The various grades of retinopathy with increasing levels of total cholesterol was statistically significant (p = 0.002.). The mean Triglyceride level increases with no evidence to severe changes of retinopathy and the difference among the progressive grades of retinopathy was statistically significant (p=0.007). Also, on Comparison of mean LDL level with several grades of retinopathy. The difference between increasing mean LDL level with severity retinopathy was found to be statistically significant (p=0.149).

In ETDRS report, Chew *et al.* told that patients with high total cholesterol and LDL levels were more likely to have retinal hard exudates when compared to patients with normal lipid profile. The patients with raised serum total cholesterol, triglyceride, LDL- C with no retinal hard exudate initially, were at increased risk of developing retinal hard exudates later [13].

The CURES study showed the association of serum lipids with DR in 1736 patients with type 2 diabetes which concluded that mean cholesterol , LDL-C and triglyceride levels were high in patients with Diabetic retinopathy when compared to those without diabetic retinopathy[14]. ETDRS study concluded that 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 which causes further progression of retinopathy [15].

A Study from France aimed to describe the influence of serum lipids on the development and progression of microvascular complications in patients with type 1 diabetes without end-stage renal disease. Finally they concluded that serum triglyceride levels were higher in patients with progressive retinal events than in those without [16].

In present study, lower the mean HDL-C level, more severe is the changes of DR and the difference was statistically significant. Global multicenter study reported that a high level of triglycerides and a low level of HDL cholesterol were associated with increased risk of diabetic microvascular diseases [17].

In our study, mean HbA1c level was less when no evidence of retinopathy and severity of retinopathy increases as the level of mean HbA1c increases. The association of mean level of HbA1c with severity of diabetic retinopathy was statistically significant (p<0.001).

Bilgin *et al.* demonstrated a correlation of lower HbA1c levels with a lower frequency of DR. Reductions in blood glucose or HbA1c concentration reduces the rate of progression of microvascular complications such as DR, neuropathy and nephropathy [18].

In the current study we have seen that mean serum cholesterol levels, mean triglyceride levels and LDL levels were significantly associated in people with diabetic retinopathy and observed to be increasing with severity of diabetic retinopathy specially advanced grades of retinopathy. The association of mean level of HbA1c with severity of diabetic retinopathy was statistically significant (p<0.001).

CONCLUSION

In our study a statistically significant correlation was obtained between severity of diabetic retinopathy with serum total cholesterol, triglycerides and LDL. There was no correlation obtained between other lipid parameters. The association of mean level of HbA1c with severity of diabetic retinopathy was statistically significant.

Dyslipidemia and glucose control are identified to be important modifiable risk factors in diabetes mellitus patients. The presence of these risk factors should warn the ophthalmologists about the need to monitor the retina. Vision impairment could be prevented which is one of dreaded complications with early diagnosis and treatment.

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