Indian Journal of Basic & Applied Medical Research; March 2012: Issue-2, Vol.-1, P. 94-102

"The Evaluation of Serum Fasting Blood Sugar and Lipid Profile including Apo A and Apo B in Diabetic Retinopathy Subjects."

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Abstract:

Background: Blindness is one of major complications of type 2 DM. The aim of this study was to evaluate the lipid profile including Apo A and Apo B levels in diabetes with and without retinopathy patients of South Indian rural population and then to correlate them.

Materials & Methods: The present study was done at PES Institute of Medical Sciences and Research, Kuppam involving in-patients and out-patients attending PESIMSR hospital. The total numbers of subjects were 90 divided into three groups. Group I- 30 healthy controls, Group II - 30 diabetes without retinopathy and Group III - 30 were diabetic retinopathy in age group between 45-75years. The investigations carried out were FBS, TC, TG, HDL-cholesterol and apolipoproteins A & B.

Results: There were increased FBS, TC, TG and Apo B levels in diabetics with and without retinopathy. Decreased levels of HDL in Group II & III were observed. Triglyceride level and Apo B levels was found to be increasing with the severity of retinopathy. Positive correlation of Apo A with HDL among diabetics with and without retinopathy.

Conclusion: Rigorous lipid control needs to be followed as it is known for health benefits, so as to prevent cardiovascular disease and ocular morbidity, thereby increasing the quality of life and vision among diabetics.

Keywords: Apolipoproteins A & B; High Density Lipoproteins (HDL); Low Density Lipoproteins (LDL)

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Introduction:

The prevalence of diabetes appears to vary between the racial/ethnic groups and its frequency will also vary [1].The mechanism by which high serum lipids may cause the progression of diabetic retinopathy is not clearly understood.

It has been postulated that elevation of blood viscosity and alteration in the fibrinolytic system occurs in hyper lipidemia causing hard exudates formation. Incorporation of triglycerides into the cell membrane leading to changes in membrane

fluidity and leakage of plasma constituents into the retina which results in hemorrhage and edema in the retina [2].

Diabetic retinopathy is characterized by macular edema and frequently accompanied by lipid exudation [3]. The most common specific complication of type 2 diabetes mellitus is the blindness. In a population based study in South India,

, diabetic retinopathy was detected in 1.78% of the patients screened and was projected to become a significant cause of blindness in the coming decade. Blindness may be due to non resolving vitreous hemorrhage, fractional retinal detachment and diabetic macular edema [4] .The retinal hard exudates are thought to be the result of lipoproteins leakage from retinal capillaries into the extra cellular space of the retina [5]. Several risk factors are associated with the development of diabetic retinopathy including hyperglycemia, arterial hypertension and elevated serum lipids, obesity and other cardiovascular risk factors [6].

Several attempts have been made to relate the large vessel diseases of diabetics to abnormalities of carbohydrate/lipid metabolism. The abnormalities of metabolism are related to microangiopathy. Some changes of lipids and carbohydrate metabolism in non-insulin dependent diabetic patients with and without retinopathy, with similar known duration of diabetes have been observed [7].

Material and Methods :

The present study was done at PES Institute of Medical Sciences and Research, Kuppam, AP, India involving in-patients and out-patients attending PESIMSR hospital. The total number of cases taken up was 90

with age & sex matched, which were divided into 3 groups. Group I included 30 normal healthy controls, Group II included 30 diabetics without retinopathy. Group III included 30 diabetics with retinopathy. All the patients included in the study were screened for the retinopathy. Retinal examination was done by Ophthalmologist.

Inclusion criteria :

Diagnosed diabetic patients with- and without retinopathy.

Exclusion criteria :

Patients with hypertension and grossly obese patients were excluded from the study.

Sample collection :

All the samples were collected after an overnight fast of 10-14 hours. 5 ml of the venous blood was collected by taking aseptic precautions. The sample was centrifuged for 15 minutes at 3000 rpm. Serum was separated. All the samples were analyzed on the same day of sample collection.

The following parameters are assessed in serum by using fully automated analyzer [Chemwell] –

1. Fasting sugar [F.B.S]
2. Total cholesterol [T.C]
3. Triglycerides [T.G]
4. High density lipoproteins [H.D.L]
5. Apo lipoprotein A [APO A]
6. Apo lipoprotein B [APO B]

Retinopathy grading is done in the following way with the help of ophthalmoscope by Ophthalmologist.

A. No evidence of diabetic retinopathy
B. Diabetic retinopathy
Non proliferative diabetic retinopathy
1. Mild NPDR
2. Moderate NPDR
3. Severe NPDR
4. Very severe NPDR

Proliferate diabetic retinopathy [PDR]
1. Low risk PDR
2. High risk PDR

Observations and Results:

TABLE: 1: Mean and Standard Deviation of Lipid Profile and FBS of Different Groups

	FBS (Mean± SD)	TC (Mean ±SD)	TG (Mean ±SD)	HDL (Mean ±SD)	LDL (Mean ±SD)	VLDL (Mean ±SD)	APO A (Mean ±SD)	APO B (Mean ±SD)
Group I [N] n = 30	95.27±14.94	167.33 ±30.28	122.13 ±38.79	41.07± 8.67	102.10 ±33.61	24.03± 7.71	114.17 ±33.28	**172.40 ±53.22**
Group II [DM] n=30	145.97± 54.18**	161.50 ±56.77	124.23 ±46.41	34.47± 6.25**	97.87± 58.00	24.50± 9.23	122.87 ±40.81	**189.20 ±54.08**
Group III [DR] n=30	**197.67± 83.39****	**180.27 ±57.70**	**161.90 ±123.5**	**34.52± 5.62****	**109.71 ±35.40**	**27.36± 15.21**	**119.13 ±41.78**	**202.93 ±48.8***

Legend-Significance *p < 0.05, **p < 0.01

In Group III [diabetic retinopathy], number of cases and its percentage of distribution in different grades are shown in Table 2.

Table : 2 : % DISTRIBUTION OF DIFFERENT GRADES IN GROUP III [DR]

	Grade 1	Grade 2	Grade 3	Grade 4
No of cases	9	13	6	**1**
% of distribution	**31**	**44**	**20**	**0.03**

The FBS, lipid profile namely total cholesterol; triglycerides, HDL, LDL, VLDL, and Apo A & Apo B were measured between different grades of Group III [Diabetic Retinopathy]. The mean and standard deviation of these values were shown in Table 3.

Table 3 : FASTING BLOOD SUGAR & LIPID PROFILE VALUES IN GROUP III WITH DIFFERENT GRADES .

	FBS (Mean± SD)	TC (Mean± SD)	TG (Mean± SD)	HDL (Mean± SD)	LDL (Mean± SD)	VLDL (Mean± SD)	ApoA (Mean± SD)	ApoB (Mean± SD)
G1	**171 ±72.4**	**184 ±36.57**	**136 ±58.26**	**36 ±4.30**	**125 ±35.47**	**26 ±10.81**	**120 ±40.3**	**175 ±33.67**
G2	**193 ±90.88***	**178 ±61.98**	**153 ±78.32***	**33 ±6.13**	**105 ±33.83**	**27 ±37.38***	**120 ±58.9**	**207 ±58.03***
G3 & G4	**199 ±89.74***	**184 ±78.43**	**229 ±221.10***	**34 ±6.53**	**131 ±26.48**	**96 ±31.47***	**121 ±20.61**	**212 ±51.32***

Legend-Significance *p < 0.05

Correlation coefficient of Apo A with HDL is done and the same is shown in Table 4

Table 4 : CORRELATION OF APO A WITH HDL :

	HDL
GROUP I [N]	**r = – 0.063 p = 0.742**
GROUP II [DM]	**r = 0.508 p= 0.004***
GROUP III [DR]	**r= 0.419 p= 0.024**

Legend - Significance * p < 0.05

Correlation coefficient of Apo B with LDL is done and the same is shown in Table 5.

Table 5 : CORRELATION OF APO B WITH LDL:

	LDL
GROUP I [N]	**r = 0.255 p= 0.175**
GROUP II [DM]	**r = 0.063 p = 0.742**
GROUP III [DR]	**r = 0.371 p = 0.052**

Discussion:

The present study demonstrates that increased serum fasting blood glucose levels in diabetcs with & without retinopathy when compared with controls. This increase is statistically significant with $p < 0.01$. Similar observation is given by others namely Tien Yin Wong et al [1] and Biljana Mijanovic et al [11].

The present study has also shown an increase in serum cholesterol, serum triglyceride levels in diabetics with and without retinopathy as compared with normal as shown in Table 1.However this variation was not statistically significant.Similar increase in triglycerides was observed by Tienyin Wong et al[1] Ishrat Kareem et al [16], Bilijanamiljaovic et al[11], Timothy. J. Lyons et al [14] and Dhir Sp Dahiya. Rajuir et al [12].

There is a significant decrease of HDL levels in diabetic retinopathy and in diabetes mellitus without retinopathy as compared to normals, which was stastically significant [$p < 0.01$]. These studies are in accordance with previous studies done by

Bilijanamil jaovic, Robert J. Glynn et al [11], Timothy. J. Lyons et al [14], Dhirsp Dahiya et al [13] and Lyons Timothy et al [17].

The reason for these lipid alterations as given by the studies are the increased free fatty acid flux associated with insulin deficiency enhances synthesis of triglycerides. The mobilization of free fatty acid from adipose tissue and their uptake by the liver increases acetyl CoA pool and this would favour an increase in cholesterol synthesis by enlarging the supply of precursors and may account for the raised plasma cholesterol [16]. ApoB present on VLDL, LDL, IDL. Apo A present on HDL. Conversion of fatty acids to triacyl glycerols and the secretion of VLDL and chylomicrons are comparatively higher in diabetics. Further the activity of the enzyme lipoprotein lipase is low in diabetic patients. Consequently the plasma levels of VLDL, chylomicrons and triglycerides are increased and hypercholesterolemia is also frequently seen in diabetics. [18].

Retinal hard exudates, which are the components of diabetic retinopathy, are most likely to be related to plasma lipoproteins, because the exudates are lipid rich. Elevated levels of these lipids conferred increased risk for future hard exudates with subsequent visual deterioration. [16] An increased Apo B level was seen in diabetic retinopathy group and in diabetes mellitus without retinopathy group as compared to normal, which was statistically significant [$p < 0.05$]. Increase in Apo B levels was also observed by Timothy. J. Lyons et al [14].

The LDL values observed in the three groups are almost similar. Similar observation of no change in the values with respect to LDL was seen in study done by Tien Yin Wong et al [1]. However, some others observed increased levels of LDL when compared between 3 such groups (Bilijanamiljaovic et al [11], Timothy. J. Lyons et al [14], Hendrika Vanleiden, Jacqueline et al [15], Bruce Gardon et al [13], Dhirsp Dahiya et al [12], Lyons Timothy et al [17].

The measurement of Apo B-100 provides information regarding the number of Apo B-100 containing particles. If the concentration of LDL cholesterol is normal or slightly increased but Apo B-100 is significantly increased, it is likely that the number of the small, more atherogenic and dense LDL particles is high.

Partial correlation coefficient among the normal with respect to Apo A, negatively correlated with HDL [7%][$r = - 0.063$]. Among the diabetes mellitus without retinopathy, Apo A positively correlated with HDL [0.04%][$r = 0.508$] but the correlation

was moderately good. Among the diabetics retinopathy Apo A positively correlated with HDL [0.2%] [r = 0.419] and the correlation was moderately good. This has been shown in the Table 4.

Among the normal Apo B has shown a positive correlation with LDL [1%] [r = 0.255] but to a lesser extent. Among the diabetes mellitus without retinopathy group, it was seen that Apo B positively correlated with LDL [7%][r = 0.063] and similarly, among diabetics with retinopathy, Apo B showed a positive correlation with LDL [0.05%][r = 0.371], the correlation being moderately good. This is shown in the Table 5.

In the current study, serum LDL, VLDL and Apo A did not show any difference in their values when compared between the 3 groups. Similar observation of no change in the values of LDL is seen in study done by Tien Yin Wong, Ronald Klein et al [1]. Some others have however observed an increased level of LDL when compared between 3 groups (Bilijanamil Jaovic et al [11], Timothy. J. Lyons et al [14], Hendrika.Vanleiden et al [15], Bruce Gardon et al [26], Dhirsp Dahiya et al [12], Lyons Timothy et al [15]. Similar study of no change in Apo A and VLDL levels are seen in studies done by Ronald Klein et al [1], Timothy. J. Lyons et al [14].

Decreased Apo A levels was expected in atherogenesis [retinopathy] but in the present study the decreased values were not seen. The probable reason may be that Apo A alterations may occur at a much later stage with the progression of the disease.

Conclusion:

The present study clearly suggest that poor control of blood sugar with dyslipidemia increases the risk for development of retinopathy. The study also reveals the association between lipoproteins, fasting blood sugar with severity and risk of retinopathy in diabetes to a certain extent.

These data lend additional support to current treatment guidelines recommending aggressive lowering of elevated lipids among diabetic patients to prevent the risk of retinopathy. Rigorous lipid control needs to be followed as it is known for health benefits, so as to prevent cardiovascular disease and ocular morbidity, thereby increasing the quality of life and vision among diabetics.

Increased Apo B-100 and decreased Apo A1 concentrations were also found in children of parents with premature atherosclerotic disease [10]. These findings suggest that apolipoproteins may be good predictors of the future CHD. The familial atherosclerosis treatment study [FATS] has demonstrated that the treatment of men young than 62 of age with documented CHD with lipid lowering agents on the basis of their Apo B-100 concentration [95th percentile .125mg/l] alone seems to be is

beneficial. A reduction in Apo B-100 concentration in these patients caused a reversal of angiogrphically demonstrable coronary atherosclerosis and reduced the incidence of clinical events. As this will be also causing arthereogenesis of retinal arteries, estimation and the lowering of Apo B-100 will be beneficial in retinopathy patients. [8]

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Date of manuscript submission:
29 October 2011
Date of initial approval:
12 December 2011
Date of Peer review approval:
2 February 2012
Date of final draft preparation:
23February 2012
Date of Publication:
2 March 2012
Conflict of Interest: Nil
Source of Support: Nil.

PISSN: 2250-284X, EISSN: 2250-2858