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Study of Glycosylated Haemoglobin and Lipid Profile in Type 2 Diabetes Mellitus with and without Retinopathy

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ABSTRACT
Introduction: *Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes. Diabetes mellitus is associated with microvascular complications, such as diabetic retinopathy (DR).A case control study was conducted to find out the relation of Glycosylated haemoglobin and serum lipids in diabetics and in diabetic retinopathy.*
Materials and Methods: *The study was done in 3 groups: diabetics, diabetics with retinopathy and normal control groups.*
Results: *The mean HbA_{1c} level , Mean values of total cholesterol, triglycerides, VLDL, LDL, were found to be significantly higher in diabetics with retinopathy and Mean values of HDL was significantly lower in diabetics with retinopathy, when compared to diabetics without complications and with normal controls.*
Conclusion: *Higher levels of HbA_{1c} and serum cholesterol, triglycerides, and LDL levels are responsible for microvascular changes in diabetes and leading to retinopathy*
Keywords: *Glycosylated haemoglobin, lipid profile, type 2 diabetes mellitus with and without retinopathy.*

Introduction

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Today, India has primary position in the global diabetes epidemiology map, which is the highest number in the world. A recent estimate suggested that Diabetes mellitus was the 5th leading cause of death worldwide. Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes. The world health organization (WHO) has projected that global prevalence of type 2 DM will be more than double, from 171 million in 2000 to 366 million by 2030[1]. Type 2 DM patients have insulin levels that appear normal or elevated but is insufficient to compensate for insulin resistance[2]. Insulin resistance reduces the capacity of myocytes to extract and store the excess glucose released from the liver[3]. Most patients of type 2 DM are obese and obesity itself causes some degree of insulin resistance[4]. Lack of insulin effect or insulin

resistance plays a primary role in metabolic derangements linked to type 2 Diabetes and hyperglycemia in turn plays an important role in disease associated complications[5]. Diabetes is a serious illness with multiple complications and premature mortality, accounting for at least 10% of total health care expenditure in many countries[6]. Diabetes mellitus is associated with microvascular complications, such as diabetic retinopathy (DR). Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20 –74 years. Duration of disease is probably the strongest predictor for development and progression of retinopathy[7]. During the first two decades of disease, nearly all patients with type1diabetes and 60% of patients with type 2 diabetes have retinopathy. The estimation of Glycated haemoglobin (GHb) has provided a dependable method of assessing glycemic control in diabetics. International Diabetes Federation (IDF 2005) guidelines advised that people with diabetes should maintain a HbA_{1c} level less than 6.5 %[8]. The determination of glycosylated hemoglobin in the management of diabetic patients was proposed by Gabbay[9] and Koenig[10] in 1976. Level of GHb is well correlated with glycemic levels over previous six to ten weeks. Higher levels of HbA_{1c} indicate a risk factor for development of microangiopathy in DM. HbA_{1c} has special affinity for O_2 and thereby it causes tissue anoxia which plays a role in causation of micro and macro angiopathy[11]. In diabetes the plasma cholesterol level is usually elevated and this causes an increased incidence of atherosclerosis and its complications. The most frequent abnormalities seen are hypertriglyceri-demia with or without hyper cholesterolemia and decreased HDL concentration. Hyperglycemia and insulin resistance play an important role in the pathophysiology of dyslipidemia in type 2 DM. More recently, the Early Treatment Diabetic Retinopathy Study (ETDRS) group and the Wisconsin Epidemiologic Study of Diabetic Retinopathy found a statistically significant association between elevated serum total cholesterol and Low-density Lipoprotein (LDL) cholesterol and the severity of retinal hard exudation in patients with diabetic retinopathy. Elevated serum cholesterol levels were significantly associated with the presence of hard retinal exudates. Since the risk of loss in visual acuity was correlated with the degree of hard exudates, which in turn might also lead to subretinal fibrosis, an intensive lipid-lowering therapy might reduce the severity of retinopathy or the resultant losses in visual acuity[12].Chronic hyperglycemia is the main etiologic factor of these complications, and thus treatment aimed towards maintaining euglycemia are the most effective means of preventing microvascular complications[13].

Materials and Methods

3 study groups were selected; 80 type 2 diabetics (with diabetic history of 10-20 yrs.), in the age group of 40-65 yrs. were included and were screened for the presence of retinopathy. Retinopathy was assessed by direct and indirect ophthalmoscopy. Exclusion criteria: Patients with history of uncontrolled hypertension, chronic diarrhoea, alcoholism, reduced renal function were excluded from the study. Methodology: Study was conducted in 120 cases with prior informed consent. Detailed history was taken [age, duration of illness, symptoms, history of hypertension, coronary heart disease, treatment taken etc.]Collection of blood samples: Blood samples were collected by venous puncture method using disposable syringes and needles under aseptic precautions and transferred into clean dry bottles. For Glycosylated Hb the whole blood specimens should be collected in a vacuum tube containing EDTA.

Statistical Analysis

The present study is designed as a case control study and statistical analysis was done to determine the difference between the groups. The results are summarized in tables and figures. Data were analyzed using Statistical Package for Social

Sciences (SPSS) version 16. Results were expressed as Mean ± SD. Mean differences between the groups were analyzed using ANOVA (Analysis Of Variance). ANOVA gives a statistical test of whether the means of several groups are all equal. Therefore it is used to test whether there is significant difference among two or more independent groups. The p value of < 0.05 will be taken as the level of significance.

Observations & Results

Table 1 Comparison of HbA_{1C} between the study groups

HbA_{1C} %				
Mean ± SD	DR	DM	Normal(NL)	p value
	-	8.1± 1.011	5.22 ± 0.655	.000*
	8.72 ± 1.334	-	5.22 ± 0.655	.000*
	8.72 ± 1.334	8.1± 1.011	-	.026*

*significant, (DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Table 2 Comparison of Total cholesterol (TC) between the study groups

TC mg/dL				
Mean ± SD	DR	DM	Normal(NL)	p value
	-	192.68±23.5	159.02±25.9	.000*
	208.7 ±19.84	-	159.02±25.9	.000*
	208.7± 19.84	192.68±23.5	-	.008*

*significant (DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Table 3 Comparison of Triglyceride (TAG) between the study groups

Triglyceride mg/dL				
Mean ± SD	DR	DM	Normal(NL)	pvalue
	-	136.5± 39.9	88.28 ± 33.6	.000*
	155.48±24.2	-	88.28 ± 33.6	.000*
	155.48±24.2	136.5± 39.9	-	.036*

*significant (DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Table 4 Comparison of HDL between the study groups

HDL mg/dL				
Mean ± SD	DR	DM	Normal(NL)	p value
	-	38.45± 7.53	42.8 ± 8.913	.039*
	32.45± 6.46	-	42.8 ± 8.913	.000*
	32.45± 6.46	38.45± 7.53	-	.002*

*significant (DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Table 5 Comparison of LDL between the study groups

LDL mg/dL				
Mean ± SD	DR	DM	Normal(NL)	p value
	-	126.9± 17.8	98.58±19.02	.000*
	145.12±20.1	-	98.58±19.02	.000*
	145.12±20.1	126.9± 17.8	-	.000*

*significant (DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Table 6 Comparison of VLDL between the study groups

VLDL mg/dL				
Mean ± SD	DR	DM	NL	p value
	-	27.32± 8.00	17.65± 6.74	.000*
	31.12± 4.96	-	17.65± 6.74	.000*
	31.12± 4.96	27.32± 8.00	-	.037*

*significant(DR-diabetic retinopathy, DM-diabetes mellitus, NL-normal controls)

Discussion

The mean HbA_{1c} levels in diabetic with retinopathy were higher than in diabetes without retinopathy and it was statistically significant (p <0.26) (Table1).The higher levels of HbA_{1c} indicate risk for development of microangiopathy in diabetics. HbA_{1c} has special affinity for oxygen and thereby causes tissue anoxia and plays a role in causation of micro and macroangiopathy. Decrease in HbA_{1c} concentrations by 1% leads to an estimated reduction of 30% in the risk of microvascular complications. Our study had also been confirmed by Boucher et al[14] who documented that levels of HbA_{1c} above 12.6% indicate a risk for development of micro-angiopathy.

The results of the present study showed a significant increase in the mean levels of total cholesterol, triglycerides, LDL, and VLDL values in diabetics with retinopathy and without retinopathy when compared to normal controls (Table2-6). There was a significant decrease in HDL cholesterol in diabetic patients, with and without retinopathy when compared to those with normal controls. Studies by Dornnan et al[15], Miccoli et al[16], Hanachi P et al[17], and Bhalla et al[18]also showed similar results.

Hypertriglyceridemia may be due to insulin resistance causing defective glucose utilization and fatty acid mobilization from adipose tissue. These fatty acids are mobilized for energy purpose and excess fatty acids are accumulated in the liver which is converted into triglycerides. Suryavanshi et al[17] suggested that insulin resistance is associated with diminished level of LDL receptor with increase in LDL particle and the resultant increase in LDL cholesterol. Individuals with type 2 DM have reduced clearance of VLDL which parallels the degree of hyperglycemia. Reduced lipoprotein lipase level in type 2 DM interfere with normal lipoprotein metabolic cascade resulting in decreased clearance of VLDL. The alterations of VLDL metabolism in type 2 DM is related in part to insulin resistance. Hyperinsulinemia and central obesity that accompanies insulin resistance also lead to overproduction and impaired catabolism of VLDL.

Decline in HDL is due to increased HDL catabolism with augmented triglyceride hepatic lipase activity. Triglyceride rich HDL particles are hydrolyzedby hepatic lipase and are rapidly catabolized and cleared from plasma. Low HDL cholesterol is often accompanied by elevated triglyceride levels, and the combination has been strongly associated with increased risk of coronary heart disease. Increased caloric intake, obesity and lack of muscular exercise also contribute to dyslipidemia observed in type 2 DM.

Dyslipidemia is also associated with the initiation and progression of diabetic retinopathy. DR was positively associated with serum triglycerides and with serum concentrations of low-density lipoprotein and apolipoprotein B (ApoB), the principal lipoprotein component of LDL. 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 alterations in the fibrinolytic system occurs in hyperlipidemia causing hard exudate formation. Life style modifications such as weight control, reduction in waist circumference, increased physical exercise, smoking cessation along with proper control of hyperglycemia and hyperlipidemia are effective interventions to ensure better quality of life, to

prevent adverse cardiovascular outcome and to retard the progression of microvascular and macrovascular complications in the long run.

Conclusions

The mean HbA_{1c} level was significantly higher in diabetics with retinopathy when compared to diabetics without complications and with normal controls.

Mean values of total cholesterol, triglycerides, VLDL, LDL, were found to be significantly higher in diabetics with retinopathy when compared to diabetics without complications and with normal controls.

Mean values of HDL was significantly lower in diabetics with retinopathy when compared to diabetics without complications and with normal controls. From the present study it can be predicted that higher levels of HbA_{1c} indicate risk for development of microangiopathy in diabetics. Thus the measurement of glycosylated haemoglobin not only shows promise of being a successful approach to the monitoring of diabetic patient but also provides a conceptual frame work for the pathogenesis of secondary sequelae of diabetes.

The results also indicate that the patients with diabetic retinopathy showed significant rise in serum cholesterol, triglyceride and LDL. Probably an increased serum cholesterol, triglyceride and LDL levels are responsible for microvascular changes in diabetes leading to retinopathy. Modification of risk factors for type 2 diabetes, might represent a novel means to prevent type 2 diabetes.

A few limitations of the current study should be noted. In the present study diabetic retinopathy grading was based on fundoscopy and not on fundus photography grading. This could have resulted in underestimation of the prevalence of diabetic retinopathy.

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