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Relationship between Glycated Hemoglobin and Serum Lipid Profile in Type 2 Diabetes Mellitus – A Case-control Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author SSS designed the study, wrote the protocol, performed the analyses of the study and wrote the first draft of the manuscript. Authors UHD and NSK managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of the study is to find whether there is any relationship between glycated hemoglobin level and serum lipid profile in type 2 diabetes mellitus patients.
Study Design: A total of 128 study participants were approached during a period 6 months of which 72 were confirmed cases of type-2 diabetes mellitus and remaining 56 were non- diabetic, and served as control subjects under the age group of 30-60 years.
Methodology: Fasting blood samples were collected from all the subjects. Body Mass index (BMI) was calculated. Fasting plasma glucose, glycated hemoglobin (HbA1c) Total cholesterol (TC), triglyceride (TG) and High Density Lipoprotein (HDL) was measured using commercially available kits. Statistical analysis was performed by use o f SPSS version l6.
Results: Plasma FBS level of diabetic group was significantly higher (p=0.001) than that of the non diabetic subjects as shown in table. TC, TG, LDL and VLDL were higher in diabetic group when compared to that of non-diabetic group, except for HDL which was lower in dian=betic group when compared to non-diabetic greoup. LDL was statistically significant between the non-diabetic and

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diabetic groups. HbA1c levels of both diabetic and non- diabetic groups showed a significant correlation with TG, HDL, LDL and VLDL ($p<0.05$) except for cholesterol.
Conclusion: The findings of this study clearly indicate that $HbA1_c$ as a useful biomarker for long-term glycaemic control and also as a good predictor of lipid profile.

Keywords: Glycated hemoglobin; diabetes; cholestrol; triglycerides; lipoproteins.

1. INTRODUCTION

India with more than 62 million diabetic individuals currently diagnosed with the disease is giving diabetes a status of a potential epidemic [1,2]. Diabetes prevalence is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a significant increase in India [3,4]. The prevalence of diabetes in India is imposing potential burden upon the country. Prevalence of disease throughout a country is affected by many factors, and identification of those factors is necessary for the facilitation of change when facing health care issues.

In India, the aetiology of diabetes is multifactorial. It includes genetic factors coupled with environmental influences such as obesity associated with rising living standards, steady urban migration, and lifestyle changes [5].

In the 1980s, HbA1c was introduced into clinical use and has become a cornerstone of clinical practice subsequently [6]. HbA1c, or glycosylated hemoglobin, is formed through the non-enzymatic binding of circulating glucose to hemoglobin (glycation) [7].

Higher levels of glucose in the blood contribute to more binding and consequent higher levels of glycosylated hemoglobin [8,9]. Because glycation occurs over the entire 90 – 120 day life span of the red blood cells, so HbA1c can be interpreted as an average of the blood glucose present over 3–4 months. Due to the representation of blood glucose in the postprandial state in addition to the fasting state, HbA1c is considered to be a comprehensive measure of total glycemic exposure than FPG, so HbA1c has been recommended for diagnosis of diabetes. There has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes recently. HbA1c acts as an indicator for the glycemic state, disease progression and development of complications in diabetic patients [10-13].

The purpose of this study is to find whether there is any relationship between glycated hemoglobin, serum lipid profile in type 2 diabetes mellitus.

2. MATERIALS AND METHODS

2.1 Ethical Clearance

This study was reviewed and cleared for human subjects by the Central Ethics Committee of Nitte University, Ref NU/CEC/Ph.D-16/2014 dated 9-10-2014.

2.2 Study Population

A total of 128 study participants were approached during a period 6 months of which 72 were confirmed cases of type-2 diabetes mellitus and remaining 56 were non- diabetic, and served as control subjects under the age group of 30-60 years, recruited from ABSMIDS and KSHEMA, Deralakatte, Mangalore.

2.3 Inclusion Criteria

- Subjects with Type 2 Diabetes Mellitus without any incidence of other systemic disorders.
- Subjects with age group between 30-60 years from both the sexes.

2.4 Exclusion Criteria

- Subjects will be excluded if they have orthopedic limitations, weight loss/gain over the previous 6 months, or any diagnosis of vascular disease, type 1 diabetes mellitus, cancer (clinically or by anamnesis), renal disease, liver disease, thyroid disease, and acute or chronic inflammatory diseases.
- Subjects consuming any medications (antihypertensive, antidyslipidemic, antithrombotic drugs).

2.5 Methods

Fasting blood samples were collected from all the subjects. Body weight and height were measured. Body Mass index (BMI) was calculated as body weight in kilograms divided by height in square meters (Kg/m^2). Fasting plasma glucose was measured by glucose oxidase method. (LyphoCHEK^{TM}AGAPPE). Glycated hemoglobin (HbA1c) was measured using Ion

Exchange Resin method on Spectrophotometer (NyoCard READER). Total cholesterol (TC), triglyceride (TG) and High Density Lipoprotein (HDL) was measured using commercially available kits (LiquiCHEK^{TM}AGAPPE). Low Density Lipoprotein (LDL) will be estimated indirectly using the Friedewald formula.

2.6 Statistical Analysis

Statistical analysis was performed by use o f SPSS versionl6 (Statistical Package for the Social Sciences). The differences between the groups were tested for significance by student's t-test and one way ANOVA test. Data were expressed as the mean±SD. P-values < 0.05 are considered statistically.

3. RESULTS

During six month study period, total 128 subjects were screened and evaluated for lipid profile. Out of 128, 72 (56%) were diabetic and 56 (44%) were nondiabetic. Nondiabetic group consisted of 46% male and 54% female and diabetic group consisted of 66% male and 34% female.

Table 1 represents the mean age, height, weight, body mass index, Fasting blood sugar (FBS), HbA1c (Glycated hemoglobin), plasma insulin and HOMA-IR values of both nondiabetc and diabetic group.

Plasma glucose level and lipid profile was measured. The mean and standard deviation (SD) of all parameter of non-diabetic and diabetic groups were compared (Table 2).

Plasma FBS (Fasting blood sugar) level of diabetic group was significantly higher (p=0.001) than that of the non diabetic subjects as shown in table (Table 2).

TC, TG, LDL and VLDL were higher in diabetic group when compared to that of non-diabetic group, except for HDL which was lower in dian=betic group when compared to non-diabetic greoup. LDL was statistically significant between the non-diabetic and diabetic groups (Table 2).

Correlation of FBS, TC, TG, HDL, LDL, VLDL with HbA1c was studied. HbA1c levels of both diabetic and non- diabetic groups showed a significant correlation with TG, HDL, LDL and VLDL ($p<0.05$) except for cholesterol (Tables 3, 4).

4. DISCUSSION

In the present study, we have evaluated the lipid profile parameters in non-diabetic diabetic individuals and correlated it with glycated hemoglobin level. Uncontrolled HbA1c level is considered to be a strong indicator of uncontrolled glucose level in blood Association of HbA1c, It is used as an indicator for the state of glycemic control, progression of the disease and development of complications in diabetic patients.

Table 1. Physical and clinical characteristics of non- diabetic and diabetic individuals

Parameters	Non-diabetic group (N=72) (M±SD)	Diabetic group (N=56) (M±SD)
Age (year)	52±11	54.8±10.8
Height (cm)	156.5±10.5	157.6±10
Weight (Kg)	60.8±12.1	63±15.8
BMI (kg/m^2)	24.7± 3.6	25.2±5.6
FBS (mg/dl)	116.8±46.5	177.3±83.3
HbA1c (%)	4.1±0.7	7.1±1.8

Table 2. Comparison of the mean lipid profile of type 2 diabetic and non-diabetic individuals

Parameters	Non-diabetic (Mean±Std. deviation)	Diabetic (Mean± Std. deviation)	'P' value
FBS (mg/dl)	116.8±46.5	177.3±83.2	**0.000**
TC(mg/dl)	214.7±83.5	222.1±77.5	0.187
TG (mg/dl)	201.8±89.8	216.2±161.2	0.206
HDL(mg/dl)	50.1±13.8	44.6±12.7	0.248
LDL(mg/dl)	124.3±83	134.2±72.2	**0.033**
VLDL(mg/dl)	40.3±17.9	43.2±12.2	0.206

Abbrevations: TC- Total Cholestrol, TG- Triglycerides, HDL- high density lipoproteins, LDL-low density lipoproteins, VLDL- very low density lipoproteins

Table 3. Correlation among HbA1c, FBS and lipid profile of non-diabetic group

Non-diabetic group	HbA1c	TC	TG	HDL	LDL	VLDL
FBS (mg/dl)	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P > 0.05	P < 0.001
HbA1c (%)	*	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
Cholestrol (mg/dl)		*	P > 0.05	P < 0.001	P < 0.001	P < 0.001
Triglycerides (mg/dl)			*	P < 0.001	P < 0.001	P < 0.001
HDL (mg/dl)				*	P < 0.001	P > 0.05
LDL (mg/dl)					*	P < 0.001
VLDL (mg/dl)						*

HbA1c-glycated hemoglobin, 'p<0.05 is statistically significant

Table 4. Correlation among HbA1c and lipid profile of type 2 diabetes group

Diabetic group	HbA1c	Cholestrol	Triglycerides	HDL	LDL	VLDL
FBS (mg/dl)	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	P < 0.001
HbA1c (%)	*	0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.05
Cholestrol (mg/dl)		*	P > 0.05	P < 0.001	P < 0.001	P < 0.001
Triglycerides (mg/dl)			*	P < 0.001	P < 0.001	P < 0.001
HDL (mg/dl)				*	P < 0.001	P < 0.001
LDL (mg/dl)					*	P < 0.001
VLDL (mg/dl)					.	*

(p<0.05) is considered statistically significant

Many studies have clearly established that complications. In patients with diabetes, are mainly due to chronic hyperglycemia. Incidence of type 2 diabetes vary between the sexes from one population to another, but these differences are relatively small and may be accounted for other risk factors like obesity and physical activity.

Increased levels of total cholesterol in diabetic group compared to non-diabetic group, may be due to an increase in the plasma concentration of VLDL and LDL, which may be due to increase in the hepatic production of VLDL or decreased removal of VLDL and LDL from the circulation. According to Suryawanshi et al. [13] higher concentration of serum cholesterol in diabetes may be attributed to decrease muscular exercise or inhibition of cholesterol catabolism increase in the LDL in diabetic patients may be due to insulin. Insulin increases the number of LDL receptor, so chronic insulin deficiency might be associated with a diminished level of LDL receptor. This causes the increase in LDL particles and result in the increase in LDL-cholesterol value in diabetes mellitus [14].

Higher levels of TG may be due to insulin deficiency which results faulty glucose utilization causes hyperglycemia and mobilization of fatty acids from adipose tissue [15].

Lower level of HDL in diabetic group compared to nondiabetic groups is attributed to triglyceride enrichment by cholesterol ester transfer protein and increased hepatic triglyceride lipase activity [16].

HDL fasters the removal of cholesterol from the peripheral tissues and hence reduces the cholesterol pool of the body. Type 2 DM is usually associated with low plasma levels of HDL [17]. Elevated levels of TG are usually accompanied by low HDL-C concentrations as seen in this study and in many others, [18] and this correlation has been strongly associated with an increase in risk of coronary heart disease (CHD) [19–21].

The study showed a strong positive correlation between elevated blood glucose concentrations and lipid parameters in both non-diabetic and diabetic individuals. The transfer of cholesterol esters from HDL-C to VLDL-C particles is increased in Hyperglycemia [22]. The denser LDL particles acquire a large proportion of these HDL esters, further diminishing the HDL-C levels. In addition, HDL-C is a ready substrate for hepatic lipase which converts it into smaller particles that are readily cleared from the plasma [23]. The relative insulin deficiency or resistance that occurs in type 2 diabetes impairs the action of lipoprotein lipase and results in lower HDL-C levels and higher TG levels, which may improve with improved glycemic control [24].

Obesity, increase calorie intake and lack of muscular exercise in the patients of diabetes

mellitus can also be a reason for high level of cholesterol, triglyceride, LDL-cholesterol and low HDL-cholesterol [25,26].

A highly significant correlation between HbA1c and FBG in our study is similar with various previous studies [27,28].

HbA1c levels of both diabetic and non- diabetic groups showed a significant correlation with TG, HDL, LDL and VLDL. HbA1c may be utilized for screening diabetic patient for risk of cardiovascular events.

Khan et al. [29] also reported that severity of dyslipidaemia increases in patients with higher HbA1c value.

Cook et al. [30] in their report on gender differences in the pattern of dyslipidemia, noted that elevated LDL-C and reduced HDL-C concentrations were commonly found in females than in males. In the present study gender wise evaluation of the data did not show any statistical significance. Similar results were also observed by Meenu et al. [31].

5. CONCLUSION

The findings of this study clearly indicates HbA_{1c} as a useful biomarker for long-term glycemic control and also as a good predictor of lipid profile. Thus, using HbA_{1c} for glycemic control monitoring help to identify diabetic patients who are at a greater risk of cardiovascular complications.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for collecting blood samples

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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