RESEARCH ARTICLE

Study of the Correlation between Total Lipid Profile and Glycosylated Hemoglobin Among the Indigenous Population of Guwahati

Debanjan Kundu[1]*, Moushumi Saikia[2], Tulika Paul[1]

[1]M. Tech Biotechnology, Amity Institute of Biotechnology, Amity University, Noida India

[2]Associate Consultant, Laboratory Medicine, Apollo Hospitals, Guwahati, Unit: International Hospital, Assam, India

[*]**Address for Correspondence:** Mr. Debanjan Kundu, M. Tech Student, Department of Biotechnology, U44/23, Room No. 8, Silver Inn PG, Sector- 24, DLF City Phase III, Gurgaon, Haryana, Gurugram- 122002, India

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ABSTRACT- In today's modern lifestyle high blood cholesterol is one of the most dreaded causes of heart diseases among the global population. Fast lifestyle, lack of exercise, obesity and improper food intake all sum up to deranged lipid profile as well as diabetes. Diabetes and high blood cholesterol go hand in hand, which leads to an increased incidence of coronary artery and cardiovascular disorders which still remains as one of the leading causes of mortality overall. In the present study there has been an effort put to draw a correlation between glycosylated hemoglobin, which is a marker for levels of blood glucose in diabetic patients as well as deranged lipid profile. Blood samples collected in sterile vials were first centrifuged and then put into analyzer for the computation of the lipid profile and the glycosylated hemoglobin. Results computed were made a note of and then prepared for statistical analysis. Results thus obtained showed that females showed significantly higher levels of total serum cholesterol and Non-HDL compared to males other than that, their lipid parameters were a little higher than males in general. Diabetic female patients showed a significantly higher level of glycosylated hemoglobin. There was a significant difference in the HDL values of patients in the pre-diabetic state and worst control of glycemic hemoglobin. There were also significant differences observed in the TGL, TGL/HDL and VLDL values between Diabetic and control patients. In general, there were an increased correlation of HbA1c with TSC and LDL and the respective ratios as HbA1c increases while LDL/HDL showed a significant increase with HbA1c.

Key-words- Cholesterol, Diabetes mellitus, Lipid profile, HDL, LDL, Lipid ratios

INTRODUCTION

Cholesterol now a day is one of the most easily recognized biological macromolecule from the perspective of human biology, mainly because of its direct relationship with atherosclerotic vascular disease [1]. The main sources of cholesterol include cheese, eggs, butter, ghee, fish, pork, chicken, and goat meat [2]. Cholesterol is absorbed from the diet and is also synthesized by the cells of the body, but mainly by the cells of the liver and intestine. The conversion step of HMG Co-A to Mevalonate is catalyzed by HMG Co-A reductase which is the rate determining step and is highly regulated by the supply of cholesterol and hence many drug targets this step for the treatment of hypercholesterolemia [3].

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An extended lipid profile includes the calculated value of very-low density lipid and triglycerides which is often checked for diagnosing hyperlipidemia. There could be various other risk factors that predispose a patient towards developing deranged lipid profiles like high blood pressure (hypertension), Type II Diabetes mellitus and a family history of developing cardiovascular disorder [4,5]. The latest third report of the National Cholesterol Education Programme (NCEP) on Detection, Evaluation, and treatment of high blood cholesterol in adults (ATP III) Ault Treatment Panel III updates the NCEP's clinical guidelines for cholesterol testing and management. The ATP III is basically an extensive and evidence based document that provides scientific rationale for the recommendations, which are contained in the document [2]. In general all the three reports on Adult Treatment Plan I, II and III extensively put thrust on LDL management through medications so as to prevent the risk of CHD in patients with high LDL levels or borderline high LDL levels [6].

Major Risk Factors modifying LDL goals [6]

- Cigarette smoking
- Hypertension (BP >140/90 or on anti-hypertensive drug)
- Low HDL Cholesterol (<40 mg/dL)
- Family History of premature CHD (Male 1st degree in <55 years of age; Women 1st degree in <65 years of age)
- Age (Men >55, Women >45 years of age)

It has often been noticed that certain diseases cause an elevated blood cholesterol levels which in turn precipitates into a sudden heart attack or death.

Diabetes is a disease which causes blood to have deranged lipid levels. High cholesterol is one of the most common problems in diabetic patients. Coronary heart disease has been perhaps singled out to be the leading cause of death in diabetic patients. Joslin, the world renowned expert on Diabetes mellitus in 1927 noted that the main reason behind development of atherosclerosis in diabetic patients is an excess of fat in body, diet and blood and this caused premature development of CAD [2]. Diabetic patients have commonly been associated with having high range of triglycerides which has also been identified as an independent factor for developing CAD. Although high cholesterol, high LDL levels and low HDL levels all result in increased risk of developing heart disease. The condition is mainly called diabetic dyslipidemia [2,7]. In fact, Triglycerides/HDL ratio correlates strongly with the incidence of CAD in both men and women [8]. In a study carried out way back in 1989, Stern *et al*. reported a study on 460 adult diabetics of which 40 per cent were seen to have deranged cholesterol levels and 23 percent had high Triglyceride/ low HDL levels [2]. Poor diabetic control is invariably associated with high levels of cholesterol and as a result, higher the levels of cholesterol higher the chances of heart disease. Other than this, hypertensions as well as obesity too are more frequently seen in diabetic patients, which also complicate the patient's condition. Kidney damage due to diabetes (diabetic nephropathy) too can cause deranged cholesterol levels in diabetic patients. Patients are also asked not to consume diet with high fats and sugar levels for good control of diabetes [2]. HbA1c test is often advised for fasting blood glucose as a marker for predicting patients who are at risk for diabetes, diabetic retinopathy or other complications of diabetes [9]. Dyslipidemia is often defined as the elevation of plasma cholesterol, triglycerides and sometimes both. Low HDL-C is also an important factor that can contribute to the development of atherosclerosis [10].

Plasma lipid and lipoprotein abnormalities as discussed have been shown to have tight correlation with type II DM [8]. This type of diabetic dyslipidemia is seen to cause atherosclerosis, cardiovascular disease and morbidity. As a result regular monitoring of FBS and HbA1c levels along with therapeutic medications are suggested to avert the result of life threatening consequences as well is imperative in effective management of diabetic dyslipidemia [11]. According to World Health Organization and American Diabetes Association (2010 & 2016), the values of HbA1c, FBS and PPBS levels are important in treatment of type II DM [11]. Many studies have also shown high levels of HbA1c are related with high incidence of cardiovascular diseases and microvascular complications such as nephropathy and retinopathy [12]. Further it has been found that elevated HbA1c levels in the pre diabetic range has also caused cardiovascular complications in general population although the underlying mechanisms have not been known [12]. Recent studies have also suggested that HbA1c levels have also been associated with large vessel disease in diabetic patients.

MATERIALS AND METHODS

In the present retrospective study, a total of 54 samples were randomly collected. The study was carried out in a tertiary care hospital in Guwahati from a period of 23rd May to 30th June, 2016. This study was both retrospective as well as introspective, hence some of the data was collected from the database of the hospital records and the remaining samples were collected and processed from the patients directly. The samples collected, specifically underwent tests for both lipid profile as well glycosylated hemoglobin (Hb%) and Fasting Blood Sugar (FBS) test. Out of the 54 patients, 44 patients were diabetic and the remaining 10 patients were chosen as control. The medical history of all the patients under this study and other secondary factors related with CVD/CAD of the same patients were collected from the Medical Records Department of the hospital after permission was granted from higher authorities.

Venous blood is mostly preferred and it is obtained by a process called venipuncture. The location from where the blood is to be collected is also important. Generally venous blood is collected from the median cubital vein in the ante-cubital fossa or the crook of the elbow. This is because the vein here is large and is close to the surface of the skin [13]. Other places might be back of the hand or the ankle although these are less desirable and should be completely avoided in patients with diabetes or poor circulation [13]. The area of collection should initially be cleaned with a sterile solution prior to the collection of the blood. The sterile solution could be 70% isopropanol and a ben-zalkonium chloride solution. After the site is cleaned it should not be touched until the venipuncture is done. The skin should be allowed to dry in air before blood is drawn so that no traces of alcohol is present as it may cause hemolysis and affect the blood test result [13].

Standardized procedure for identifying the link between the patient and the sample is usually done by the serial number or the patient's identification number which is used throughout the chain from sample collection to result processing. For this purpose there are various procedures for automatic identification and data collection purposes. In many clinical laboratories labeling with a bar code has

become quite significant choice of technology for the purpose of automatic identification [13]. The tests are performed in Automated Chemistry Analyser Dimension Rxl for lipid profile and D10 (BIORAD) for HbA1c.

All the statistical analysis of the various raw data collected was performed using statistical software MINITAB version 17. After the collection of the data, raw data was converted to a tabulated form. Statistical analysis included basic descriptive statistics of all the components followed by computation of Pearson's correlation coefficient (r) between: HbA1c and all other components and FBS and all other components. The analysis was further strengthened by computing the respective p-values and also 1-tailed Student's t test. The conclusion was drawn henceforth. The strength and significance of two correlations was tested using the Fisher r-to-z transformation using sociostatistics.com and vassarsstats.net respectively. The other data that was collected was of the entire medical history which was also looked for various parameters specially the history related to the principal diagnosis and preexisting diagnosis specially focusing on T2DM and hypertension. A separate statistical analysis was performed for them representing the data in the form of graphical illustrations.

RESULTS

All the raw data collected from the hospital records and also computed directly from the patient's sample were put forward for a complete statistical analysis in order to gain a quantitative outlook of the theoretical data. As mentioned earlier, a total of 54 patients were taken into consideration for this study with a male: female ratio of 34:20 of which 44 patients were found to be diabetic based on the results of the HbA1c and FBS values. The remaining 10 patients were chosen as control. The present study was a mix of both retrospective and introspective data.

Table 1: The number of Patients distributed category wise lipid profile

Category	Number (%)
Total number of patients	54
Hypercholesterolemia (>200 mg/dL)	12 (22.20)
Hyper LDL-C (>100 mg/dL)	25 (46.29)
Hypertriglyceridemia (>150 mg/dL)	23 (42.59)
Hypo HDL-C (<40 mg/dL)	36 (66.66)
Mid HDL-C (>40mg/dL-<60 mg/dL)	13 (24.07)
High HDL (>60 mg/dL)	5(9.25)
Non HDL-C (>160 mg/dL)	12 (22.20)
Hyper VLDL (>30 mg/dL)	23 (42.59)

Table 2: Total number of diabetic patients and their lipid profiles

Category	Number (%)
Total number of diabetic patients	44
Hypercholesterolemia (>200 mg/dL)	10 (22.72)
Hyper LDL-C (>100 mg/dL)	21 (47.72)
Hypertriglyceridemia (>150 mg/dL)	22 (50.00)
Hypo HDL-C (<40 mg/dL)	31 (70.45)
Mid HDL-C (>40mg/dL-<60 mg/dL)	9 (20.45)
High HDL (>60 mg/dL)	4 (9.09)
Non HDL-C (>160 mg/dL)	10 (22.72)
Hyper VLDL (>30 mg/dL)	22 (50.00)

Table 3: Gender-wise distribution of the data on the basis of Diabetes mellitus

Category	Males (%)	Females (%)
Total number of Diabetic patients	27/34 (79.41)	17/20 (85)
Hypercholesterolemia	4/27 (14.81)	6/17 (35.29)
Hyper LDL-C	11/27 (40.74)	10/17 (58.82)
Hypertriglyceridemia	12/27 (44.44)	10/17 (58.82)
Hypo HDL-C	19/27 (70.37)	12/17 (70.58)
Mid HDL-C	7/27 (25.92)	3/17 (17.64)
Hyper HDL-C	1/27 (3.70)	2/17 (11.76)
Hyper Non HDL-C	4/27 (14.81)	6/17 (35.29)
Hyper VLDL	12/27 (44.44)	10/17 (58.82)

Table 4: Comparison of parameters between Diabetic and Control Patients

Control	Diabetic
HbA1c= 5.33±0.41	8.19±2.27
FBS=107.8±19.52	191.7±70.2
TSC=160.7±36.7	163.77±43.43
LDL=98.25±30.39	96.86±33.69
HDL=37.60±13.2	36.35±16.03
TGL=114.5±35.3	170.0±83.2
TGL/HDL=3.5±1.8	5.51±3.56
TSC/HDL=4.38±1.52	5.20±2.1
LDL/HDL=3.03±1.29	3.09±1.57
Non-HDL=123.05±31.49	127.19±42.66
VLDL=22.92±7.08	34.00±16.64

We observe the basic descriptive statistics related to the data collected initially based on the gender compared to the overall statistics of all the data. This analysis is followed by the analysis based on the various groups formed based on the glycemic control of the patient. The glycemic controls of the patients were divided into three categories: Prediabetic (<6.5%), Diabetic (6.5–9.0%) and Uncontrolled Diabetes (> 9%). In order to gain a full proof conclusion with regards to this study, it was important to look at the various angles of the data collected. The respective p-values as well as t-values for the computed correlation coefficient as well as means of the various parameters were calculated so as to see the significance of the values obtained. The confidence interval (C.I) was taken to be 95% and the p-value to be <0.05 at α=0.05.

Once we assess the overall means, standard deviations and range of all the patients and compare the values first on the basis of gender, we observe the overall mean of HbA1c is 7.66±2.33, FBS is 179.30±73.16, TSC is 163.56±42.06, LDL is 97.36±33.04, HDL is 37.9±16.61, TGL is 158.9±79.7, TGL/HDL is 5.1±3.4, TSC/HDL is 5.049±2.012, LDL/HDL is 3.07±1.49, Non-HDL is 128.49±41.52 and VLDL is 31.74±15.91. There is no significant difference of the HbA1c, FBS levels between males and females although females have higher values of the same compared to males. Females have significantly higher levels of Total Serum Cholesterol (t=-2.16, p=0.017) and Non-HDL (t=1.9, p=0.02 at p<0.05) compared to males. Among other lipid parameters, females have higher value compared to males but they are not statistically significant. There is significant difference in the HbA1c and FBS levels between the three groups of patients (t = -10.15, p<0.00001, t = -7.469, p<0.00001, t = -11.24, p<0.00001) There is significant difference in the HDL-C (t=1.86774, p<0.035) levels between the Pre-Diabetic patients and patients with worst glycemic control.

There is significant difference (t = -1.71, p= 0.047) in the TGL/HDL ratio between the Pre-Diabetic patients and Diabetic patients with poor glycemic control. There is significant difference in the TGL and VLDL levels between Diabetic patients with poor glycemic control and patients with uncontrolled diabetes (worst glycemic control). There is a significant difference in HbA1c (t=3.94, p=0.0001) FBS (t=3.72, p=0.00024) TGL (t=2.05, p=0.022) TGL/HDL ratio (t= -1.79, p=0.047) and VLDL (t= -2.05, p=0.02266) between diabetic patients and the control patients.

Significant correlation between HbA1c and FBS (p-value= <0.0000) at p=0.05. No significant correlation between HbA1c and TSC, LDL, TGL, but the highest positive correlation is between HbA1c and LDL although there are weak positive correlations between HbA1c and TGL/HDL, TSC/HDL and LDL/HDL, which suggests that the lipid ratios in diabetic patients could be used as a marker for the risk of CVD/CAD. Although not significant but FBS shows a higher positive correlation between itself and TSC, LDL and TGL compared to glycosylated Hb.

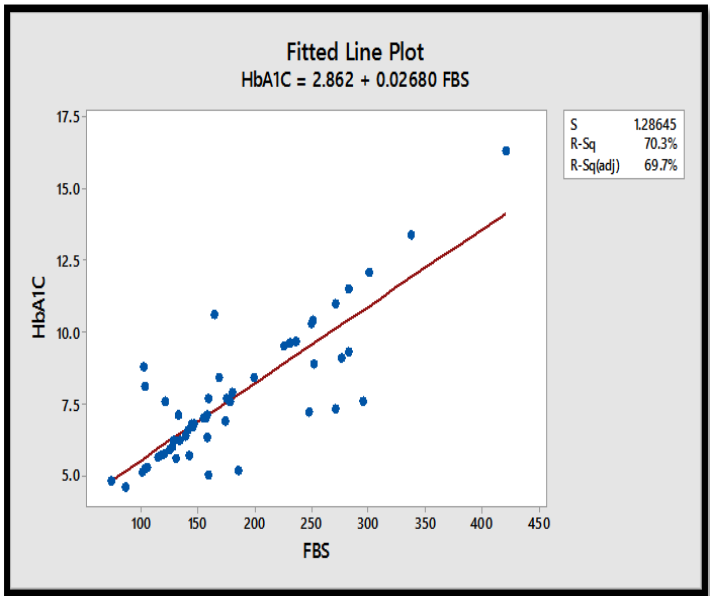

Fig. 1: A regression fitted-line plot for the overall correlation between HbA1c and FBS

When we assess the correlation between HbA1c, FBS and all the parameters based on gender we observed, females show a significant higher correlation between HbA1c and FBS (z=1.95, p=0.025) compared to males. Females also have a higher correlation between HbA1c and the lipid ratios as well as the FBS and the Lipid ratios compared to males. The strongest correlation is shown between HbA1c and LDL/HDL ratio between the two genders although they are not significantly high.

Comparison between the diabetic patients and the control group leads us to find a 1) a significant higher correlation (z=1.65, p=0.04) between HbA1c and HDL in non-diabetic patients than diabetic patients. The lipid ratios are also much lower in non-diabetic patients than the diabetic patients although they are not significant.

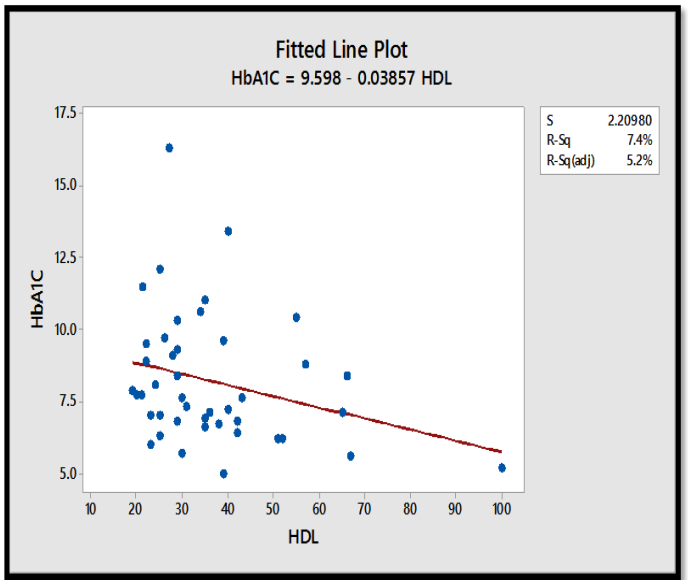

Fig. 2: Inverse Correlation between HbA1c values and HDL

After assessing the various correlation coefficient of HbA1c, FBS with all other parameters, it is see that there is a significant increase in the correlation between HbA1c and FBS between Group II and Group III (p=0.005, z= -2.56). In general the correlation between HbA1c and TSC, LDL & FBS and TSC, LDL show increase with higher HbA1c levels, in other words with poor glycemic control. There is a significant decrease in the levels of HDL-C between Groups I and Group III (p=0.09, z=1.3). The HDL-C levels also decrease in Group II, compared to Group I, although not significantly.

The lipid ratios also show higher correlation with HbA1c levels as it increases suggesting that lipid ratios could be a very good marker for prediction of CAD/CVD in diabetic patients. There is a significant increase (p=0.031, z= -1.86) in the correlation between LDL/HDL and FBS between Group I and Group III, suggesting that it could be most important marker of predicting CAD/CVD. Patients with the worst glycemic control have the worst lipid profiles and hence have a more risk of running into CAD/CVD.

DISCUSSION

In the present study we have tried to establish the most important lipid parameter that is affected in patients with poor and worst glycemic control. The study was done keeping in mind the high prevalence of the same in today's world. Our overall mean of HbA1c reported in this study is in agreement with previous studies [8,11,12]. Similar FBS levels have also been reported in [8]. The overall TSC and LDL levels as found in our study were within normal ranges which have been reported earlier [2]. The levels of HDL reported here is in agreement with Gupta *et al*. for the average HDL levels among Indians. Similar results have also been reported [11] and [8] further reported a similar number of patients suffering from hypercholesterolemia and hypertriglyceridemia as reported in our study. It has also been reported in a study that patients with type II diabetes had higher occurrence of hypertriglyceridemia and hyper LDL [14] and [15]. The study also reported that there were no significant difference in the HbA1c and FBS levels between males and females similar to our findings and further reported that females had a significantly higher level of total serum cholesterol than males which has again been seen in our study too [14]. Significant differences in the HbA1c levels among the three groups of patients have also been reported in [12]. Significant difference in the HDL-C levels between non-diabetic and diabetic patients have also been reported in [11]. Small inverse correlation between HbA1c and LDL in our study is in agreement with [11]. Our study is in agreement with the study of [10] in concluding that non HDL cholesterol can be a better predictor of CVD in diabetic population. The correlation between HbA1c and glucose levels found in our study is in agreement with [15,16]. Obesity is also considered to be one of the most important factors diabetes and impaired glucose regulation [16].

CONCLUSIONS

After completion of this study, it is very much clear that Type II Diabetes mellitus will increase the chances of developing diabetic dyslipidemia as a major complication which in turn will make the patient more prone of developing major cardiovascular complications in due course of time. Although common people should also know that most of these complications are treatable and that heart conditions are reversible. In order to take a good control of the poor lipid profile and glycemic condition of oneself, patients should make some necessary changes in lifestyle including food habits and personal habits like smoking and alcohol consumption. Along with these patients should also indulge in some good amount of physical activity which has always proven to have an overall effect on blood cholesterol. Patients with a family history of hypertension, diabetes or premature CAD/CVD or having symptoms of metabolic syndrome should take special medical assistance with immediate effect. Obese patients should watch the body weight and keep it within measures.

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