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Research Article

AN INSIGHT INTO THE LIPID ABNORMALITIES IN TYPE 2 DIABETES MELLITUS PATIENTS IN VELLORE REGION, SOUTH INDIA

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ABSTRACT

Objective: The objective of the present study is to evaluate the pattern of lipid profile parameters and correlate with HbA1C in Type 2 diabetes mellitus (T2DM) subjects of Vellore region, South India.

Methods: 286 clinically diagnosed Type 2 diabetic patients were included for this study. Fasting blood samples were collected for HbA1C, blood glucose and lipid profile estimation.

Results: Only 139 of the total patients studied (n=286) had good glycemic control (HbA1C values < 7 %, Group A) and the remaining 147 had HbA1C values > 7 % (Group B), indicating relatively poor glycemic control. The total cholesterol, triglycerides and non-HDL values (mg/dl) for group A were 174.3 ± 28.7, 165.9 ± 67.9 and 135.5 ± 29.3 and for group B, they were 189 ± 44.6, 203 ± 93.4 and 145.2 ± 45.4.

Conclusions: The values of both the groups were above the target values recommended by the NCEP-ATPIII guidelines. The correlation of HbA1C with triglycerides was found to be more significant than correlation with other lipid parameters. Patients with good glycemic control exhibited more favorable (20.1%) blood lipid levels (none out of target) than those with poor glycemic control (6.1%). This data indicate that HbA1C can be used as a biomarker for establishing mixed dyslipidemia in T2DM. Our study indicates substantial underachievement of treatment goals by diabetic patients in both the groups.

Keywords: HbA1C, Hyperglycemia, Lipid abnormalities, Mixed Dyslipidemia, T2DM.

INTRODUCTION

India is experiencing an epidemic of diabetes. The global estimate of this disease was 2.8% in 2000, with a projected increase to 4.4% in 2030 [1] and in India about 80 million people are expected to suffer from diabetes during this time. With the rising number of people diagnosed with diabetes, a significant rise in the number of complications also is expected. The deleterious effects of hyperglycemia on patients with type 2 diabetes have been studied extensively [2]. Both type 1 and type 2 diabetes are associated with an increased risk of cardiovascular diseases [3].

In India 52.2% deaths due to Cardiovascular diseases (CVD) occur below the age of 70 years, whereas this percentage in developed countries is only 22.8% [4]. Metabolic risk factors for type 2 diabetes mellitus (T2DM) and its associated complications include hypertension, dyslipidemia, hyperglycemia and abdominal obesity [5]. Although lipid profile, blood pressure and glucose levels before and after meals are routinely measured by clinicians, target levels for lipid profile parameters are not achieved in many cases. Hence an understanding of the prevalence of dyslipidemia in type 2 diabetes and the measures taken to control the same are vital.

Glycated hemoglobin (HbA1C), a routinely used marker for long term glycemic control, predicts the development of complications in diabetes [6]. Recently, elevated HbA1C has been shown as an additional risk factor for CVD in subjects with or without diabetes [7]. The influence of hyperglycemia and dyslipidemia on the development of complications in diabetes has been thoroughly studied [8, 9].

In India, many studies were carried out to estimate the prevalence of diabetes and the complications associated with it [10, 11]. However, to our knowledge, no study has been carried out to establish the correlation between hyperglycemia and lipid abnormalities in T2DM subjects in Vellore region. Therefore, we undertook this study to assess the patterns of lipid abnormalities and correlate with glycemic control (HbA1C) in T2DM subjects.

MATERIALS AND METHODS

A total of 286 type 2 diabetic patients with either sex (173 males and 113 females), ranging from 21 to 80 years of age, who were registered between 16th January, 2011 and 15th June, 2011 in the outpatient department of Medzon Diabetes Center, Vellore, Tamil Nadu, were included in this study. Patients were diagnosed to have type 2 diabetes based on their medical history, clinical examination and previous laboratory investigations [12].

The patients were asked to follow their routine diet, physical exercise and usual medications. Venous blood samples were collected from all the subjects after at least 8 hours of fasting with their informed consent. Fasting total cholesterol (TC), triglycerides (TG) and High density lipoprotein (HDL) were estimated by "End Point Biochemistry" method. The serum Low density lipoprotein (LDL) concentration was calculated using the Friedwald and Frederickson formula, LDL-C = TC – (HDL-C + TG/5) mg/dL [13]. Glycemic control was assessed by the estimation of HbA1C using ion exchange chromatography [14].

Fasting blood glucose (FBG) and 2 hours post prandial blood glucose levels (PPBG) were estimated by glucose oxidase method [15]. Value of HbA1C was given as percentage and values of all other parameters were given in mg/dL. The Institutional ethical clearance and patient's consent was obtained for this study.

Based on the HbA1C values, they were divided into two groups. Those subjects who had optimal glycemic control were classified as Group A [HbA1C lesser than or equal to 7] and those who did not have good control as Group B (HbA1C more than 7). According to NCEP-ATP III guidelines, the clinically recommended target values for total cholesterol, triglycerides, LDL-C and non-HDL were < 200, < 150, < 100, and < 130 mg/dL respectively. For HDL the target value is > 45 for men and > 55 for women [16]. Dyslipidemia was defined by the presence of one or more values "out of target". Lipid profile data were analyzed separately for both the groups and correlated with HbA1C.

Statistical analysis: The values were compared by student's t-test and the results were considered significant when p value ≤ 0.05.

RESULTS

The general characteristics and biochemical parameters of the entire study population are listed in Table 1.

Table 1: Comparison of clinical and biochemical parameters in male and female T2DM patients

Characteristics	Men[n = 173]	Women [n = 113]
Age (yrs)	52 ± 12.2	49.8 ± 10.4
HbA1C	7.4 ± 1.1	7.2 ± 0.9
FBG, mg/dL	133 ± 55	130 ± 53
PPBG, mg/dL	208 ± 68	199 ± 80
Total cholesterol, mg/dL	183 ± 40	180 ± 35
Triglycerides, mg/dL	189 ± 88	182 ± 77
HDL-C, mg/dL	43.3 ± 4.9	44.4 ± 4.7
LDL-C, mg/dL	102.4 ± 37.8	135.4 ± 33.1
Non-HDL-C, mg/dL	140 ± 41.1	135 ± 35.7
Cholesterol/HDL-C ratio	4.3 ± 1.1	4.1 ± 0.9
Dyslipidemia, %	74	65

Values are mean ± SD

Two hundred and eighty six patients comprising of 173 (60.4%) males and 113 (39.6%) females with type 2 diabetes were included. Mean age and SD of the patients were 52 ± 12.2 and 49.8 ± 10.4 for males and females respectively.

The present study exhibited an increased prevalence of dyslipidemia in diabetic men (74%) as compared to diabetic women (65%).

Table 2 shows the comparison of biochemical parameters between group A and group B.

Table 2: Comparison of biochemical parameters in group A and group B

Parameters	Group A HbA1C < 7 [n = 139]	Group B HbA1C>7 [n = 147]	P-value
FBG, mg/dL	94 ± 13.1	167 ± 54	< 0.001
PPBG, mg/dL	157.6 ± 24.1	254 ± 69.6	< 0.001
Total Cholesterol, g/dL	174.3 ± 28.7	189 ± 44.6	< .0.001
Triglycerides, mg/dL	165.9 ± 67.9	203 ± 93.4	< 0.001
HDL-C, mg/dL	43.7 ± 4.6	43.6 ± 5.2	0.865
LDL-C, mg/dL	97.3 ± 27.6	104.6 ± 42.2	0.915
Non-HDL-C, mg/dL	130.5 ± 29.3	145.2 ± 45.4	< 0.001
Cholesterol/HDLC ratio	4.0 ± 0.9	4.4 ± 1.3	0.134

Values are mean ± SD

Only 139 (48.6%, 80 males and 59 females) patients had good glycemic control (HbA1C < 7) and the remaining 147 (51.4%, 93 males and 54 females) patients showed poor glycemic control (HbA1C > 7). FBG and PPBG values of Group B were significantly higher as compared to Group A. An increase in total cholesterol, triglycerides and non-HDL was observed in both the groups. However, the values of total cholesterol, triglycerides and non-HDL [mg/dL] were relatively lower in group A [174.3 ± 28.7, 165.9 ± 67.9 and 135.5 ± 29.3] as compared to the group B values [189 ± 44.6, 203 ± 93.4 and 145.2 ± 45.4]. No statistically significant differences were observed in the mean of HDL/LDL and TC/HDL ratios between the two groups. Non-HDL values in Group B showed a sharp increase over Group A. The mean atherogenic index value (cholesterol/HDL ratio) of group B was 4.4 implying a multifold risk of atherosclerosis [17].The prevalence of dyslipidemia based on the number of values out of target is presented in Table 3.

Table 3: Distribution of dislipidemia in diabetic men and women of Group A and Group B

Particulars	Men		Women		Total [n=286]
	Group A [n = 78]	Group B [n = 95]	Group A [n = 61]	Group B [n = 52]	
a) None out of target:					
a-1] Non-HDL-C < 130 + HDL-C ≥ target + TG < 150	18	4	10	5	37[12.9]
b) One out of target:					
b-1] Non-HDL-C ≥ 130	6	14	5	5	30[10.5]
b-2] HDL-C < target	7	3	8	11	29[10.2]
b-3] TG 150 – 400	11	16	9	9	45[15.7]
c) Two out of target:					
c-1] Non-HDL-C ≥ 130	5	14	4	4	27[9.4]
+ HDL-C < target	9	12	13	10	44[15.4]
c-2] Non-HDL-C ≥ 130 + TG 150 - 400	6	11	9	8	34[11.9]
c-3] HDL-C < target + TG 150 - 400					
d) Three out of target:					
d-1]Non-HDL-C ≥ 130 + HDL-C < target + TG 150 - 400	12	17	3	8	40[14]

Values in parentheses are percentage of total number of patients

Patients with good glycemic control exhibited more favorable (20.1%) blood lipid levels (none out of target) than those with poor glycemic control (6.1%). The prevalence based on One Out Of Target Value namely TG > 150, Non HDL > 130 and HDL < target (45 for men and 55 for women) is 33.1 for Group A and 32 % for Group B. The prevalence based on Two Out Of Target Values namely TG > 150 + Non HDL > 130, TG > 150 + HDL < target (45 for men and 55 for women) and Non HDL > 130 + HDL < target for Group A and Group B is 33.1 and 37 % respectively. The prevalence based on Three Out Of Target Values namely TG > 150 + Non HDL > 130 + HDL < target (45 for men and 55 for women) for Group A and Group B is 6.4 and 21 % respectively.

DISCUSSION

The present study evaluated the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1C. The Centre for Disease Control and Prevention recently reported that 70 to 97% of individuals with diabetes have dyslipidemia [18]. Hence, a new term, termed diabetic dyslipidemia, has been used and it correlates low HDL and high triglycerides with postprandial lipidemia. Those who are in the prediabetic state also exhibit a similar lipid profile pattern because of their association with insulin resistance [19]. Normalizing circulating lipid levels has been shown to reduce cardiovascular complications and mortality [20, 21].

The levels of HbA1C and FBG did not differ significantly between male and female diabetic patients (Table 1). There was no marked variation in the mean lipid values of male and female subjects. The lipid profile data analyzed for the 286 subjects showed that the mean TC and LDL remained in the optimum range. The type of lipid abnormality in diabetes depends upon many factors such as type of diabetes, endogenous insulin reserve, Body Mass Index, medications and the presence or absence of other complications such as

nephropathy. Data from Hazara division showed higher LDL levels in Type 2 diabetics [22]. Studies from various parts of India reveal differences in the prevalence of lipid abnormalities in diabetic patients [23, 24]. Increased serum cholesterol and low HDL were reported from studies on Northern India [25].

Comparing the lipid profile data of controlled (group A) and uncontrolled diabetics (group B), it was found that the levels of TC, TG and non-HDL showed statistically significant difference (Table 2). However, the HDL level remained below target in both the groups. The TC/HDL ratio of group A and Group B were 4.0 and 4.4 respectively. The correlation of HbA1C with triglycerides was found to be more significant than correlation with other lipid parameters. These data suggest that uncontrolled type 2 diabetics exhibit undesirable lipid values much more than controlled diabetics. The UKPDS, United Kingdom Prospective Diabetes Study, is a clinical trial of intensive control of blood glucose after diagnosis of T2DM [26]. In the intensive treatment group of that study, each 1% reduction in mean of HbA1C was associated with a 14% reduction of myocardial infarction. Therefore, effective control of hyperglycemia is imperative for preventing diabetic complications. The results of the DCCT [Diabetes Control and Complications Trial] study suggest that strict blood glucose control has long lasting benefits associated with reduced cardiovascular events in patients with type 1 diabetes, years after the treatment period [27]. The present study also reveals a high non-HDL-cholesterol level in group B. The non-HDL level is highly correlated with the level of apolipoprotein-B and is a better predictor of Coronary Artery Disease risk than LDL in patients with elevated TG (≥ 200mg/dL, 28). Therefore, non-HDL goals have been established as secondary targets for patients with elevated triglycerides by the National Cholesterol Education Program [NCEP, 16]. But our study proves that achieving optimum levels of Non-HDL values is not taken up fully into clinical practice. LDL has been designated as the primary target of therapy since the late 1980s and hence non-HDL which is included in the current guidelines is not yet treated aggressively.

Assessment of total cardiovascular risk is important and it is the first step in the management of dyslipidemia. Though dyslipidemia is a major modifiable risk factor for CVD, complex dyslipidemias have been shown to be present and they are not only difficult to diagnose, but also have unpredictable response to therapeutic interventions. In the present study, diabetic patients were divided into two groups as per the HbA1C cut off value of value 7%. HbA1C was established as the Gold Standard of glycemic control by the Diabetes Complication and Control Trial [DCCT]. Table 3 depicts the number of dyslipidemics in diabetic men and women of group A and group B based on three different criteria, namely one out of target, two out of target and three out of target. Patients with good glycemic control (20.1%) exhibited more favorable blood lipid levels [none out of target] than those with poor glycemic control (6.1%). No difference was observed between men and women of group A and group B based on one out of target. However, a significant difference was noticed between these two groups of men and women based on two out of target and three out of target. The percentage of dyslipidemic diabetic women (present in group A and group B) was significantly higher in two out of target group than men. On the contrary, more men were found to present in the three out of target group than women. The prevalence of dyslipidemia in group B was higher (93 %) compared to group A (79 %).

CONCLUSION

Diabetic patients with elevated HbA1C and mixed dyslipidemia are considered as a high risk group for CVD. Substantial reduction of cardiovascular deaths in diabetics can be achieved by improving glycemic control [6, 29]. Our data indicate that HbA1C can be used as a biomarker for establishing mixed dyslipidemia in T2DM. Further, these data indicate substantial underachievement of treatment goals by diabetic patients in both the groups. The lower frequency of treatment success in both groups indicates that more aggressive treatment is needed to reach NCEP goals. Our study data is consistent with the national emphasis on reduction of cardiovascular mortality due to abnormally high levels of lipid parameters among diabetics. Larger epidemiological studies are required to study the link between the various factors of CVD and glycemic control of T2DM patients.

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