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Original Research Article

Effect of varying glycated hemoglobin level on lipid profile in patients with type 2 diabetes

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Abstract: Chronic hyperglycemia in diabetic patients is often associated with long term complications like diabetic nephropathy, neuropathy, retinopathy and heart diseases. An abnormal lipid level is considered as the most common factor for heart disease and is responsible for higher mortality due to its complications. Now, glycated hemoglobin (HbA1c) has been accepted as a biochemical marker for long term blood glucose concentration and also a measure for development of complications caused due to diabetes mellitus. For every rise in 1% of absolute HbA1c the possibility of having heart diseases increases by 18% hence, rigid glycemic control with HbA1c <7% is recommended for the diabetic patients. This study was designed to compare the lipid profile levels in patients with type 2 diabetes mellitus not on lipid lowering drugs depending on their HbA1c levels. One hundred and ten patients of type 2 diabetes mellitus were divided into four groups based on their HbA1c levels: HbA1c ≤ 6.9% (n= 20), HbA1c 7-8.4% (n= 40), HbA1c 8.5 – 9.9% (n= 15) and HbA1c ≥ 10% (n= 35). Fasting lipid profile was estimated by dry chemistry analyzer (Vitros 250) and HbA1c was estimated by high performance liquid chromatography (Biorad D10). In our study, we found that patients with HbA1c level ≥10% i.e., very poor glycemic control had significantly lower good cholesterol (HDL) levels. Also, LDL/ HDL and TC/ HDL ratios were higher in patients with very poor glycemic control. The findings of our study indicate that type 2 diabetic patients with HbA1c ≥ 10% are at higher risk of developing cardiovascular diseases. Timely intervention can prevent complications due to diabetes by strictly monitoring lipid profile along with HbA1c levels.
Keywords: cardiovascular disease, diabetes mellitus, glycated hemoglobin, HDL-cholesterol, strict glycemic control

INTRODUCTION

Diabetes mellitus is a metabolic disease continuously increasing in both developed and developing countries [1]. According to International Diabetic Federation (IDF) report, total number of diabetics in South-East Asian population was found to be 78 million in 2015 and was expected to rise to 140 million by the year 2040 [2]. India was announced as the "Diabetic Capital of the World" by World Health Organization (WHO) because of continuous rise in population with diabetes mellitus [3,4]. Diabetes mellitus is a clinical condition characterized by increased blood glucose level due to defect in insulin secretion, insulin action or both. Type 2 diabetes mellitus is less severe than type 1 diabetes and accounts for 90 – 95% of all diagnosed cases. In type 2 diabetes the hormone insulin is present in sufficient amount but cannot be utilized by the body. In diabetic patients chronic hyperglycemia is often associated with long term complications like diabetic nephropathy, neuropathy, retinopathy, and heart diseases [5]. In type 2 diabetes, abnormal lipid level is considered as the most common factor for cardiovascular disease (CVD) and is responsible for higher mortality due to its complications [6-8]. According to American Heart Association updated on 26 Jan 2016, 68% of patients of >65 years with diabetes die due to heart diseases [9].

Glycated hemoglobin (HbA1c) arises from non-enzymatic attachment of hexose molecule to the amino terminal valine residue of β-chain of hemoglobin and reflects the average plasma glucose level of previous 2-3 months. Till 1977, HbA1c was not used as an indicator of gylcemic control [10], however in 1993

the Diabetes Control and Complications Trial (DCCT) and 1998 the United Kingdom Prospective Diabetes Study (UKPDS) provided the evidence that over the last 30 years HbA1c has gained an importance in monitoring the diabetes [11,12]. In agreement with its function as an index for average blood glucose level, HbA1c predict the risk of complications in patients with diabetes mellitus. Now, HbA1c has been accepted as a biochemical marker for long term blood glucose concentration and also a measure for assessing the risk of complications caused due to diabetes mellitus. The level of HbA1c is directly proportional to the blood glucose concentration and reflects the average blood glucose levels of previous 8-10 weeks [13]. According to Selvin et al for every rise of 1% in HbA1c the possibility of having heart diseases increases by 18% [14]. To reduce the risk for cardiovascular complications, patients with diabetes are advised to manage the level of HbA1c below 7% [15]. In view of information available from various studies, one or the other parameters of lipid profile were found to be related with HbA1c level in type 2 diabetic patients [16-20]. Thus, this study was planned to find out the effect of varying HbA1c level on lipid profile in patients with type 2 diabetes mellitus not on lipid lowering drugs.

MATERIAL AND METHODS

One hundred and ten patients of type 2 diabetes mellitus age between 35 – 86 years with at least one year history of diabetes on treatment but not on lipid lowering drugs presented to the outpatient department of King George's Medical University, Uttar Pradesh Lucknow India over a period of 3 months were enrolled in the study. Out of 110 patients, 60 (54.55%) were males and 50 (45.55%) were females. Patients were divided into four groups on the basis of HbA1c levels; A: HbA1c ≤ 6.9% (excellent control), B: HbA1c 7 – 8.4% (good control), C: HbA1c 8.5 – 9.9% (poor control) and D: HbA1c ≥ 10 % (very poor control).After obtaining informed consent from the patients, blood sample were taken under aseptic precautions and analyzed in Department of Biochemistry. Fasting blood samples were collected for total cholesterol (TC), triglyceride (TG), High-Density Lipoprotein (HDL) and analyzed by using Vitros 250 (dry chemistry analyzer). Very Low Density Lipoprotein (VLDL) and Low Density Lipoprotein (LDL) were calculated by Friedwald equation (VLDL=TG/5; LDL= TC-VLDL-HDL). Ratios of TC/ HDL and LDL/ HDL were also calculated. HbA1c was estimated by National Glycohemoglobin Standardization Program (NGSP) certified HPLC method (Bio-rad D10). Based on the cut-off provided by National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guidelines lipid levels were taken as abnormal i.e. total cholesterol >200mg/dl as hypercholesterolemia, triglyceride >150mg/dl as hyper-triglyceridemia, good cholesterol i.e. HDL <40mg/dl, LDL cholesterol >100 mg/dl, TC/HDL >4.5 and LDL/HDL >2.5. The data was summarized as mean ± SD by using SPSS 18.00. One Way Analysis of Variance (ANOVA) and Tukey's Test was used to analyze the data in between the groups. P value < 0.05 was considered as statistically significant.

RESULTS

The study comprised of 54.55% males (n=60) and 45.45% females (n=50) and no difference was observed in their HbA1c levels. The mean levels of HbA1c were 6.33 ± 0.22 in group A (excellent glycemic control), 7.61 ± 0.46 in group B (good control), 9.12 ± 0.41 in group C (poor control) and 11.81 ± 1.40 in group D (very poor glycemic control). Mean level of total cholesterol (F= 0.60; P= 0.61), triglyceride (F= 0.55; P= 0.64), VLDL (F= 0.40; P= 0.75) and LDL ((F= 1.19; P= 0.31) were not statistically different in four groups. However, mean level of HDL cholesterol were significantly lower in group D with very poor glycemic control (ANOVA F= 3.33; P = 0.022) as presented in Table [1].

Mean levels of HDL cholesterol were significantly lower in group D when compared to group B (P = 0.018 by Tukey's test). Ratio of TC/ HDL (F= 4.15; P= 0.008) and LDL/ HDL (F= 4.44; P= 0.006) were significantly higher in group D as compared to other groups as presented in Table [2]. Statistical significant difference were observed for TC/ HDL and LDL/ HDL ratios (P= 0.005; 0.003) between group B and group D.

No statistical significant difference for TC (χ^2= 1.14; P= 0.76), TG (χ^2= 2.04; P= 0.58), VLDL (χ^2= 1.37; P= 0.71), LDL (χ^2= 5.96; P= 0.11), TC/ HDL (χ^2= 3.33; P= 0.34) and LDL/ HDL (χ^2= 2.95; P= 0.39) ratios were observed in patients with abnormal lipid profile in four groups according to NCEP ATP III guidelines. However, HDL cholesterol were found to be lower in 66.7% patients of group C with poor glycemic control which was statistically significant (χ^2= 8.08; P= 0.044) when compared with cut-off defined by NCEP ATP III. In group D, 62.8% patients were found to have significantly lower HDL cholesterol as presented in Table [3].

Table-1: Lipid profile and average blood glucose in four groups

Group	N	TC Mean ± SD	TG Mean ± SD	HDL Mean ± SD	VLDL Mean ± SD	LDL Mean ± SD	Average blood glucose
A	20	135.55±48.01	144.80±63.86	36.95±17.62	28.75±12.74	73.95±34.60	134.45±6.42
B	40	149.40±45.52	146.65±78.51	45.72±17.18	29.80±16.36	71.32±31.38	171.20±13.21
C	15	150.46±38.68	160.06±51.22	36.60±13.86	31.73±10.17	82.00±34.87	214.80±12.09
D	35	153.11±53.49	164.80±74.82	34.42±15.70*	32.65±14.87	86.00±38.36	296.08±53.50
***F**		0.60	0.55	**3.33**	0.40	1.19	**143.30**
****P**		0.61 (NS)	0.64 (NS)	**0.022 (S)**	0.75 (NS)	0.31 (NS)	**<0.001 (S)**

*F-value in one way ANOVA

** P-value is the calculated probability

Table-2: Ratio of TC/HDL and LDL/HDL in four groups

Group	TC/HDL Ratio	LDL/HDL Ratio
A	4.38±1.80	2.33±1.21
B	3.59±1.50	1.81±1.07
C	4.80±2.49	2.57±1.37
D	5.22±2.46	2.91±1.59
F	**4.15**	**4.44**
P	**0.008 (S)**	**0.006 (S)**

Table-3: Patients with abnormal lipid profile in accordance to NCEP ATP III

	A	B	C	D
TC	1 (5%)	5 (12.5%)	2 (13.3%)	5 (14.3%)
TG	7 (35%)	15 (37.5%)	6 (40%)	18 (51.43%)
HDL-c	12 (60%)	14 (35%)	10 (66.7%)*****	22 (62.86%)
VLDL	4 (20%)	9 (22.5%)	3 (20%)	11 (31.43%)
LDL	5 (25%)	5 (12.5%)	6 (40%)	11 (31.43%)
TC/HDL	9 (45%)	11 (27.5%)	5 (33.3%)	16 (45.71%)
LDL/HDL	10 (50%)	13 (32.5%)	8 (53.3%)	16 (45.71%)

DISCUSSION

In our study, mean HbA1c levels were not statistically different between males and females in all the four groups which is similar to the findings of earlier studies performed by Haseeb and Doruk et al [21,22]. Mean level of TC, TG, VLDL and LDL were not significantly different in four groups. However, in patients with very poor glycemic control i.e. HbA1≥ 10%; the good cholesterol levels (HDL) were significantly lower when compared to patients with excellent, good and even with the patients with poor glycemic control. In group D patients, the ratios of TC/ HDL and LDL/ HDL which are considered to be an accurate predictor of coronary heart disease were significantly higher when compared to other groups [23,24]. In 2001, study conducted by Lemieux et al reported TC/HDL ratio as a better marker compared to LDL/HDL for predicting the risk of ischemic heart disease [25]. Our finding is in accordance with Lemieux et al, TC/HDL ratio is much higher as compared to LDL/HDL ratio in all the four groups which may predict the chance of developing heart disease in diabetic patients. Studies are available which show that HbA1c has inverse association with HDL and a direct association with cholesterol, triglycerides and the bad cholesterol (LDL) i.e. as the level of HbA1c increases the level of HDL decreases while there is an increase in cholesterol, triglycerides and LDL cholesterol [21,26]. Study conducted by Mahato et al in patients with HbA1c >7% compared with other group having HbA1c <7%, observed significant higher levels of cholesterol, triglycerides, bad cholesterol, LDL/ HDL and TC/ HDL in patients with HbA1c value > 7%. However, no statistically significant difference was observed in mean level of good cholesterol between two groups in their study [27]. Similarly study conducted by Samatha et al on patients with HbA1c > 7% showed direct and significant correlation with FBG, TC, LDL, LDL/HDL ratio as compared to patients with HbA1c < 7%, while no significant difference were found in mean level of triglyceride and HDL [28].

In our study HDL-cholesterol level were significantly lower and ratio of TC/HDL were quite higher in type 2 diabetic patients with very poor glycemic control (HbA1c ≥10%) as compared to patients with excellent, good glycemic control and even with the patients having HbA1c between 8.5% – 9.9%.

HDL cholesterol and ratio of TC/HDL are known predictor of coronary heart disease thus we can predict higher risk of having heart diseases in patients with HbA1c ≥10% as compared to other groups.

As diabetes mellitus is an epidemic in South East Asian population, more studies should be conducted on large population size so that early interventions could be taken to prevent cardiovascular disease in type 2 diabetic patient with poor glycemic control. The upper age limit taken in our study was 86 years which could be reduced in future studies as significant decrease in various lipid components (TC, TG, LDL) were seen with advancing age in earlier studies.

CONCLUSION

According to present study it can be concluded that strict glycemic control and monitoring of lipid profile level will lower the chance of having heart diseases and also the death rate in diabetic patients.

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