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The association between serum lipids profile and HbA$_{1c}$ in type 2 diabetes mellitus in Tehran, Iran

Fatemeh Mehravar[1], Mohammad Ali Mansournia[2], Moussa Abolhassani[3], Kourosh Holakouie-Naieni[2], Ensie Nasli-Esfahani[4*]

[1]Clinical Research Development Unit (CRDU), 5 Azar Hospital, Golestan University of Medical Sciences, Gorgan, I.R. Iran; [2]Epidemiology and Biostatistics Dept., Tehran University of Medical Sciences, Tehran, I.R. Iran; [3]Student Research Committee, Shahroud University of Medical Sciences, Shahroud, I.R. Iran; [4]Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, I.R. Iran.

Original article

ABSTRACT

Background and aims: Dyslipidemia is one of the major factors implicated in the development of the vascular complications of diabetes. In this study, it was evaluated the association between serum lipids profile and Hemoglobin A$_{1c}$ (HbA$_{1c}$) in type 2 diabetes mellitus.

Methods: In this cross-sectional study, the serum lipid profile and HbA$_{1c}$ was studied on 562 Iranian patients who were older than 30 years and had type 2 diabetes identified from the diabetes and metabolic diseases clinic of endocrinology and metabolism research institute. A Multiple Linear Regression analysis was also done with the HbA$_{1c}$ as outcome variable and serum lipids profile as predictor variables; adjusted for potential confounders (age, sex, diabetes duration and Body Mass Index (BMI)).

Results: In 1966, 6.34% of the national total population was over 60 years compared to mean age of the participants that was 61.6±10.4 years, with a range of 32 to 89 years. The results confirmed that the Triglyceride (TG) (β: 0.11, 95% CI: 0.000-0.004, P=0.01) and cholesterol (β: 0.13, 95% CI: 0.000-0.009, P=0.04) were correlated with the HbA$_{1c}$ value but there were no significant association between HDL and LDL.

Conclusion: This study demonstrated that in persons with type 2 Diabetes Mellitus (DM), HbA$_{1c}$ value is a good predictor of lipid profile. Therefore, lipid profiling for all persons with type 2 DM should be a routine test.

Keywords: Lipid Profile, Diabetes, Dyslipidemia, Triglycerides, HbA$_{1c}$.

INTRODUCTION

Diabetes mellitus is a global health issue affecting children, adolescents, and adults. According to the World Health Organization, the number of people with diabetes has risen

*Corresponding author:** Ensie Nasli-Esfahani, Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, I.R. Iran, Tel: 00989128937199, E-mail: mehravar10261@yahoo.com

from 108 million in 1980 to 422 million in 2014.[1] The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.[2] Dyslipidemia is a major systemic disorder and one of the important risk factors for cardiovascular disease. According to Adult Treatment Panel (ATP) III Guidelines At-A-Glance dyslipidemia is elevation of plasma cholesterol, TG, or both, or a low high-density lipoprotein level that contributes to the development of atherosclerosis.[3] Many of reason cause elevated TG in patient with DM type 2; one reason is the enzyme that transport of free fatty acid cross the plasma membrane is Hormone Sensivit Lipse (HSL). Insulin inhabit HSL, insulin resistant in patient with uncontrolled type 2 DM cause activation HSL and increase fatty acid and transport free fatty acid from adipose tissue to liver and produced Very Low-Density Lipoprotein (VLDL) and increase TG.[4]

Dyslipidemia is a powerful risk factor for coronary heart disease.[3] Although DM and dyslipidemia are two separate risk factors for atherosclerosis, the results of many studies on patients with type 2 DM show that diabetes and dyslipidemia have a whole range of pathophysiological overlaps and that these interactions accelerate the process of atherogenesis.[5,6] The purpose of control of dyslipidemia in diabetic patients is Low-Density Lipoprotein Cholesterol (LDL-C) with a target level of <80 mg/dL (2.0 mmol/L).[6]

The role of hyperglycaemia in Cardiovascular Disease (CVD) is supported by a direct correlation between fasting blood glucose and cardiovascular events.[7,8] Impaired lipid metabolism resulting from uncontrolled hyperglycemia has been implicated in cardiovascular complications in diabetes patients. Published reports suggest that the type 2 diabetes are associated with plasma lipid and lipoprotein abnormalities.[9,10] All of dyslipidemia features is associated with an increased risk of cardiovascular disease in diabetes patients.[11]

Glycated (HbA$_{1c}$), as a reflection of glycaemia, is an important indicator of glycemic control for the previous 3 months.[12] Previous studies have not conclusively demonstrated that HbA$_{1c}$ is an indicator for dyslipidemia and cardiovascular disease in type 2 diabetes patients.[8,13,14] In this study, the purpose of the current study was to examine the association between serum lipids profile and HbA$_{1c}$ in type 2 diabetic patients in Tehran between January and April 2014.

METHODS

In this cross-sectional study, we evaluated the clinical characteristics of 562 Iranian diabetic patients (older than 30 years and had type 2 diabetes) who were admitted to the diabetes and metabolic diseases clinic of endocrinology and metabolism research institute in Tehran between January and April 2014, were enrolled in the study.

Inclusion criteria were age greater than 30 years, type 2 diabetes (controlled or uncontrolled and with or without complications) and diabetes duration more than 5 years. Patients were excluded from the study if they were pregnant, had severe and enduring mental health problems, were not primarily responsible for their own care and refused to participate in the study or were participating in another research study.

A checklist was administered from patient records regarding demographic information (sex, age, BMI, ethnicity, marital status, and education), current diabetes treatment (use of oral hypoglycemic agents and insulin), the duration of diabetes, and the presence of diabetes complications. The outcomes were serum lipids profile (TG, Cholesterol, HDL, and LDL) and HbA$_{1c}$, ascertained from clinical patient records.

The protocol of this study was reviewed and approved by the Tehran University of Medical Sciences Institutional Ethical Review Committee. Informed consent was obtained from all of the subjects prior to the examinations.

The quantitative and qualitative data were described as mean (standard deviation) and frequency (percentage), respectively. Pearson correlation coefficients were calculated to estimate relations between serum lipids profile and HbA$_{1c}$ in type 2 diabetic patients. In addition, a multiple linear regression analysis was also done with the HbA$_{1c}$ as outcome variable and serum lipids profile as predictor variables; adjusted for potential confounders (age, sex, diabetes duration and BMI). Stata software, version 12 (Stata Corp, College Station, TX, USA) was used for all statistical analyses.

RESULTS

Of 600 patients who were invited, 562 (93.7%) cases accepted to participate. The mean (SD) age of the participants was 61.62 (10.49) years, with a range of 32 to 89 years. Of 562 subjects, 232 (41.3%) were male. The mean (SD) duration of the illness was 12.82 (6.61) years and the mean (SD) BMI of the participants was 27.85 (4.38) kg/m^2, with a range of 18.1 to 47.4 kg/m^2. There are 264 (47.0%) patients with no complications of diabetes. Also, the prevalence of retinopathy, neuropathy and nephropathy complications of diabetes was 28.1%, 17.4%, and 14.2%, respectively as shown in Table 1.

Table 1: Description of the population and association with HbA$_{1c}$ level (n=562)

Characteristic		n(%)	P
Sex	Male	232(41.28)	0.24
	Female	330(58.72)	
Marital status	Single	17(3.02)	0.74
	Marriage	463(82.38)	
	Widow	82(14.59)	
Education	Less than high school	186(3.09)	0.02
	High school graduate	102(18.15)	
	At least some college	161(28.65)	
	College graduate or beyond	113(20.11)	
Age (years)	30-44	30(5.34)	0.65
	45-59	209(37.19)	
	60-74	254(45.20)	
	75-90	69(12.28)	
Diabetes duration (years)	< 5	45(8.0)	0.04
	5-9	172(30.6)	
	10-14	141(25.1)	
	≥ 15	204(36.3)	
BMI	Underweight	6(1.1)	0.68
	Normal or healthy weight	141(25.1)	
	Overweight	257(45.7)	
	Obese	158(28.1)	
Nephropathy	Yes	482(85.77)	0.11
	No	80(14.23)	
Neuropathy	Yes	464(82.56)	0.38
	No	98(17.44)	
Retinopathy	Yes	403(71.71)	0.02
	No	159(29.29)	

Glycosylated (HbA$_{1c}$) level in 48% of patients was less equal 7.5%, 31.1% between 7.6-8.9% and the rest is more equal 9.0% (Table 2).

Table 2: Associations between serum lipids profile and HbA$_{1c}$ with Chi-squared test (unadjusted)

	HbA1c	≤ 7.5%	7.6-8.9%	≥ 9.0%	P
TG	Low risk (<150 mg/dL)	173	98	57	0.01
	Borderline (150-199 mg/dL)	49	48	28	
	High risk (≥200 mg/dL)	48	29	32	
Cholesterol	Low risk (<200 mg/dL)	243	158	91	0.001
	Borderline (200-239 mg/dL)	20	13	13	
	High risk (≥ 240 mg/dL)	7	4	13	
HDL	Low risk (> 60 mg/dL)	222	16	9	0.89
	Borderline (35-45 mg/dL)	121	89	58	
	High risk (<35 mg/dL)	34	20	18	
LDL	Low risk (<130 mg/dL)	254	165	100	0.01
	Borderline (130-159 mg/dL)	11	7	7	
	High risk (≥160 mg/dL)	3	2	7	

The TG (β: 0.11, 95% CI: 0.000-0.004, P=0.01) and cholesterol (β: 0.13, 95% CI: 0.000-0.009, P=0.04) were correlated with the HbA$_{1c}$ value but there were no significant association between HDL and LDL in adjusted linear regression models as shown Table 3.

Table 3: Associations between serum lipids profile and HbA$_{1c}$ in adjusted linear regression models

HbA$_{1c}$	*Adjusted Beta coefficient (95 % CI)	P
TG	0.11(0.000 to 0.004)	0.01
Cholesterol	0.13(0.000 to 0.009)	0.04
HDL	-0.055(-0.008 to 0.002)	0.19
LDL	0.010(-0.005 to 0.006)	0.86

: Adjusted for age, sex, diabetes duration, BMI.

Figures 1 indicate the Pearson correlation between serum lipids profile and HbA$_{1c}$ in type 2 diabetic patients and the relationship between cholesterol (r=0.162, P<0.001), TG (r=0.152, P<0.001) and LDL (r=0.117, P=0.006) levels with HbA$_{1c}$ was significant.
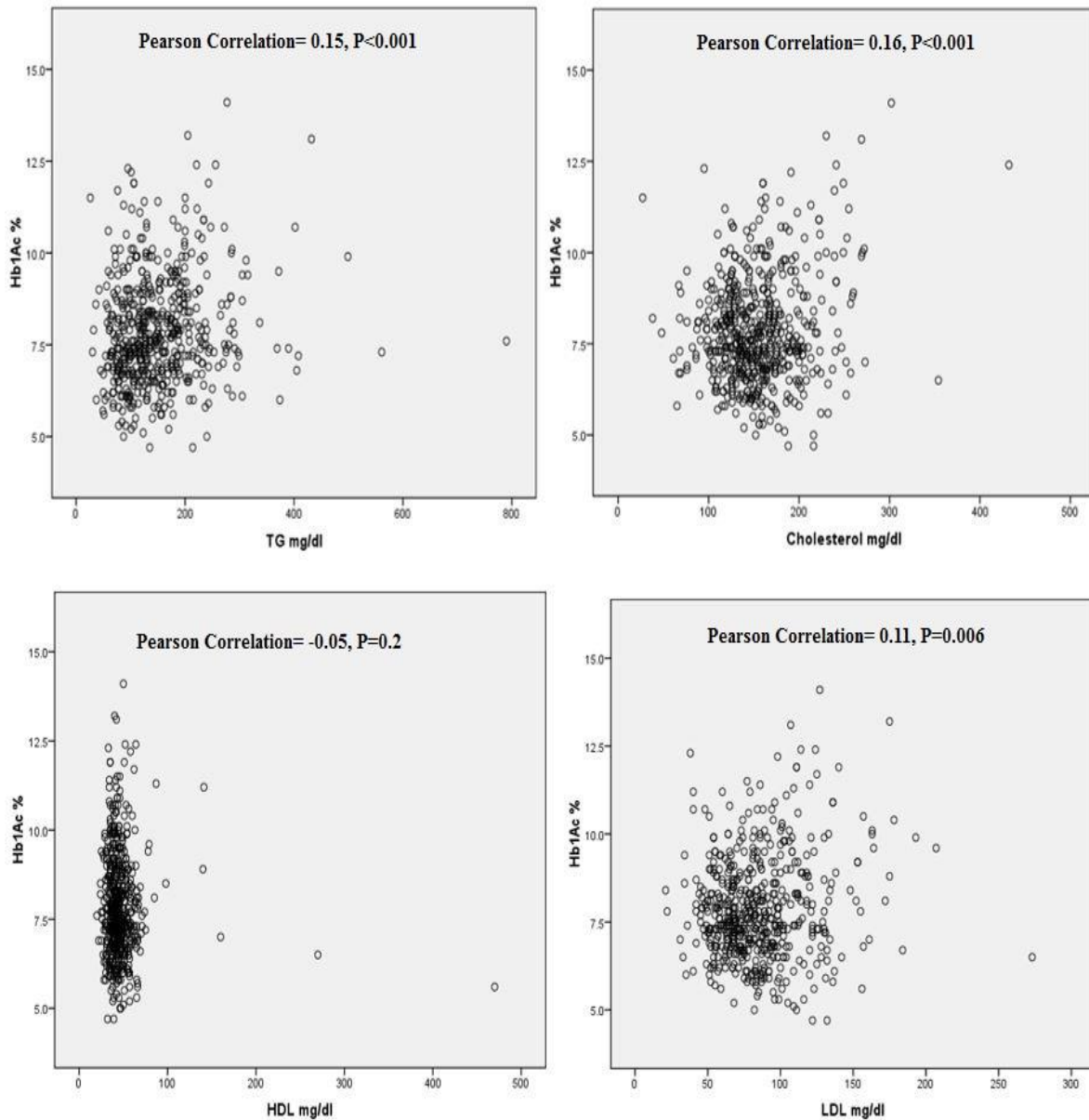
Figure 1: Pearson correlation between serum lipids profile and HbA1c in type 2 diabetic patients

DISCUSSION

In the present study, we have evaluated the serum lipids profile in in type 2 diabetes mellitus subjects and its correlation with HbA_{1c}. The results of this study showed that the levels of HbA_{1c} are not affected by patients' gender, marital status, age and BMI, But the significant correlation between HbA_{1c} and age is in agreement with earlier reports.[15,16] In this study, the levels of HbA_{1c} was significant correlation with level of education (P=0.02) and Diabetes duration (P=0.04).

We also surveyed the correlation between HbA_{1c} with the prevalence of retinopathy, neuropathy and nephropathy complications of diabetes. The results

showed that the prevalence of retinopathy was correlation with level of HbA$_{1c}$. Morton and et al inspected the relationship amongst HDL and micro vascular (renal and retinal) infection in an accomplice of 11140 patients with type 2 diabetes. Amid postliminary, 32% of the patients grew new or exacerbating miniaturized scale vascular malady, and 28% encountering a renal occasion and 6% a retinal occasion.[17]

We also surveyed significant correlations between HbA$_{1c}$ and cholesterol, TC, LDL and HDL ratio. In various studies, HbA$_{1c}$ level was eminent as showing positive correlation with TC, LDL and TG in diabetic patients.[18-20] Our study showed a significant correlations between HbA$_{1c}$, cholesterol and TG in diabetic patients which is in agreement with the findings of several other investigators who reported significant correlations between HbA$_{1c}$ and lipid profiles and suggested the importance of good management of diabetes in controlling dyslipidemia.[21-23] The similarly more grounded relationship of HbA$_{1c}$ than FBG with lipid profile is upheld by a prior study reporting higher connection coefficients for HbA$_{1c}$ than irregular glucose, for example, cholesterol, TG and LDL.[24] We did not watch huge connections between HbA$_{1c}$ with HDL and LDL. Be that as it may, in some past studies, it was critical connections.[25,26]

In the present study, we divided diabetic patients into 3 groups according to their HbA$_{1c}$ levels: Group 1: Good glycemic control (HbA$_{1c} \leq 7.5\%$); group 2: Poor glycemic control ($7.5\% \leq$ HbA$_{1c} \leq 8.9\%$) and group 3: Worst glycemic control (HbA$_{1c} \geq 9\%$). Though there was no significant differences in HDL in 3 groups with regard to glycaemia control, alterations in other lipid parameters were statistically significant in three different groups.

The diabetic patients with poor glycaemia control displayed a huge increment in cholesterol and TG and with no huge modification in HDL and LDL. Prior, it was seen that type 2 diabetic patients without CHD had the same HbA$_{1c}$ levels independent of sex while female patients with CHD had higher HbA$_{1c}$ than particular male controls.[27] Diabetes presents an extraordinarily expanded danger of CHD occasions in both ladies and men.[28] In any case, ladies with diabetes seem to have encountered with an expanded CHD mortality.[29] Diabetic ladies might be liable to more unfriendly changes in coagulation, vascular capacity and CHD hazard variables than diabetic men.[30,31] Note that diabetic patients kept on being at expanded danger of CHD if their HDL levels remain problematic regardless of effective diminishments of LDL with statin treatment.[32] Be that as it may, vulnerability to CVD among type 2 diabetic patients varies extraordinarily as per ethnicity and sex.[33]

Seriousness of dyslipidemia increments in patients with higher HbA$_{1c}$ esteem. As hoisted HbA$_{1c}$ and dyslipidemia are autonomous danger components of entanglements of diabetes, diabetic patients with raised HbA$_{1c}$ and dyslipidemia can be considered as a high hazard bunch for inconveniences of diabetes. Enhancing glycemic control can significantly decrease the danger of cardiovascular occasions in diabetics.[34] It has been assessed that lessening the HbA$_{1c}$ level by 0.2% could bring down the mortality by 10%.[35]

The present study confirms the TG and cholesterol were correlated with the HbA$_{1c}$ value, but there were no significant association between HDL and LDL. In conclusion, we demonstrated that in persons with type 2 DM, HbA$_{1c}$ value is a good predictor of lipid profile. Therefore, lipid profiling for all persons with type 2 DM should be a routine test.

The benefits of current study are including: Significant volume of cases and

accuracy in choosing of cases. In other hand, this study is done on patients of referral clinic of Tehran University of Medical Sciences and these cases are representing the statistic society of diabetic patients of Tehran.

CONCLUSION

This study demonstrated that in persons with type 2 DM, HbA_{1c} value is a good predictor of lipid profile. Therefore, lipid profiling for all persons with type 2 DM should be a routine test.

For further studies, it is suggested to do these actions with analytic and interventional methods that give us this ability to control variables that are responsible for bias and find their real relation.

CONFLICT OF INTEREST

Fatemeh Mehravar, Mohammad Ali Mansournia, Moussa Abolhassani, Kourosh Holakouie-Naieni, Mina Khanhosseini and Ensie Nasli-Esfahani declare no conflict of interest. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This study obtained its ethics approval from the Ethical Committee of Tehran University of Medical Science. Informed consent was obtained from all individual participants included in the study.

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