Original Article

A Survey on the association of glycosylated hemoglobin A1C and hyperlipidemia in patients with type 2 diabetes

Hadis Musavi[1], Mojdeh Mahdiannasser[2], Amir Shamshirian[3], Soheil Azizi[4*]

[1]Department of Biochemistry, Faculty of Basic Science, Razi University Kermanshah, Iran
[2]Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
[3]Department of Laboratory Sciences, Student Research Committee, School of Allied Medical science, Mazandaran University of Medical Sciences, Sari, Iran
[4]Department of Laboratory Sciences, School of Allied Medical science, Mazandaran University of Medical Sciences, Sari, Iran.

Received: 12 September 2017; Accepted: 12 April 2018

Abstract

Background: Type 2 diabetes includes a series of disorders characterized by hyperglycemia, which are followed by dysfunction in insulin secretion. In the clinical laboratory, A1C test defines blood glucose levels over a three-month period. The aim of this study is to evaluate the correlation between HbA1c and hyperlipidemia in patients with type 2 diabetes. **Materials and Methods:** An cross-sectional study was performed on 209 diabetic patients men (n=109) and women (n=100) with a mean age of 57.1 ± 11.1 years. Diagnosis of diabetes was performed according to the WHO criteria. In this study, venous blood (5 ml) was collected from participants after overnight fasting, and HbA1C levels and lipid profiles were determined using enzymatic methods and auto-analyzer device. Risk factor values (TCH/HDL-C) and atherogenic index of plasma (AIP) (logTG/HDL-c), as well as LDL-C/HDL-C ratio, were calculated. **Results:** HDL-C and TCH / HDL-C were significantly increased in women. On the other hand, LDL-C/HDL-C and HbA1c levels were significantly higher in men. There was no significant difference in the levels of cholesterol, triglyceride, fast blood sugar (FBS), LDL-C, and AIP between women and men. Cholesterol, FBS, LDL-C and LDL-C/HDL-C also showed a significant direct correlation with HbA1c, but no significant correlation was observed between triglyceride, HDL, AIP, and risk ratio with HbA1c. **Conclusion:** HbA1c may be considered as a biomarker for dyslipidemia screening in patients with type 2 diabetes.

Keywords: Diabetes; lipid profile; Glycosylated hemoglobin (HbA1C); Atherogenic index.

***Corresponding Author:** Soheil Azizi, Department of Laboratory Sciences, School of Allied Medical science, Mazandaran University of Medical Sciences, Sari, Iran, E-Mail: soheil_azizi@yahoo.com, (Tel): +98911-111-9989.

Please cite this article as: Musavi H, Mahdiannasser M, Shamshirian A, Azizi S. A Survey on the association of glycosylated hemoglobin A1C and hyperlipidemia in patients with type 2 diabetes. Arch Med Lab Sci. 2018;4(1):9-14.

Introduction

Diabetes is one of the most significant diseases in the U.S. and is one of the problems of today's human societies(1). Diabetes mellitus (DM) is a metabolic syndrome caused by defects in secretion or dysfunction of insulin(2). Oscillations of lipid profiles occur as a result of DM and due to these alterations, distribution and function of various lipids are affected (3). Type 2 diabetes (T2DM) is a complex condition with low levels of HDL-C and increased levels of triglycerides and LDL-C. These are the main features of insulin resistance syndrome, which is seen in most patients with diabetes. In fact, individuals predisposed to diabetes have shown high levels of lipid profiles such as cholesterol, triglycerides, LDL-C, and low levels of HDL-C(4) World Health Organization (WHO) investigations estimate that the number of patients with diabetes has risen from 135 million in 1995 to 300 million in 2025 . According to the International Federation of Diabetes (IDF) in 2013, more than 3.4 million people were diagnosed with diabetes in Iran and the prevalence in

adults of 20-79 years was 43.8%. In addition, about 38002 individuals died from diabetes and up to the now, approximately 2198 patients with diabetes in Iran have not been statistically diagnosed(5). Hemoglobin A1C (HbA1c) is an important indicator of long-term glycemic control over a period of two to three months and is extensively used for treatment decisions in clinics(6). Hb Glycation, the incorporation of non-enzymatic glucose into the amino group of protein is irreversible and is correlated with Hb lifespan and blood glucose concentration. This measurement indicates blood glucose levels over the last 6-8 weeks(7). There is a direct correlation between HbA1c and diabetes complications(8). Coronary artery disease (CAD) is one of the major reasons for mortality in patients with non-insulin dependent diabetes (NIDDM)(9). In several experiments, the risk factors for CAD in patients with diabetes were specified and increased levels of total cholesterol, LDL-C, VLDL-C, and HDL-C were decreased compared to controls(1). Previous studies have shown that HbA1c level can not only be used as a long-term indicator of blood glucose but also as a high level of HbA1c with an increased risk of cardiovascular disease and mortality(10).

Therefore, continuous monitoring of HbA1C in patients with diabetes as well as consumption of glucose-lowering drugs can improve the risk of complications regarding hyperglycemic control(11). It is also recommended that HbA1c and glycemic control should be evaluated every 3 to 6 months(12). Today, the key target in the treatment of patients with diabetes is to achieve a level of less than 7% (optimal control) since it is linked to reduced mortality(13). According to the aforementioned points, proper glycemic and lipid profile control in patients with diabetes can lead to a dramatic improvement of awareness and reduce the cost of treatment. In this study, we investigated a group of patients with T2DM who referred to Bouali hospital in Sari to evaluate serum lipids , HbA1c levels, and the possible correlation among them. Furthermore, the association of atherogenic index of plasma (AIP) with HbA1C and risk ratio (TCH / HDL-C) were investigated.

Methods

This analytical cross-sectional study was conducted from February 23 to May 31, 2018, at Bouali Hospital with the approval of the Ethics Committee of Mazandaran University of Medical Sciences. All necessary information in patients' profiles was employed considering Ethical Principles of Helsinki, and on the basis of non-probability sampling. 209 patients with diabetes, including men (n=109) and women (n=100), were selected. Diagnosis of diabetes was performed according to WHO criteria. Accordingly, a fasting blood glucose level of ≥126 mg/dL or 2 hours glucose (2hPG) ≥196 mg/dL was indicative of diabetes. Cases did not use alternative therapies with hormone or vitamin supplements. Moreover, patients consuming tobacco and alcohol, as well as cases of the following conditions were excluded from the study: chronic diseases of kidney, liver, and lung; acute inflammatory diseases (especially acute pancreatic and endocarditis infections); heart valve disease; short stomach allergy syndrome; immunodeficiency; pregnancy and lactating women. Blood samples were collected and the levels of HbA1C, HDL-C, LDL-C, TCH, and TG were determined using enzymatic methods (Auto-analyzer). Eventually, the values of the ratio of LDL-C/HDL-C and the risk ratio of TCH/HDL-C as well as Atherogenic Index of Plasma (AIP) were calculated. To compare the mean of two or more groups, t-test and ANOVA were used respectively. Furthermore, Pearson correlation test was used to examine the linear correlation of variables. All tests and statistical analyses were performed using SPSS16 software.

Results

The mean age for all people was 57.1 ± 11.1 years. The average was 56.1 ± 9.9 for women and 58.1 ± 11.8 years for men. There was no significant difference in the mean age between men and women ($P > 0.05$). The mean HbA1C level and lipid profiles of men and women, as well as the total mean of patients, are shown in Table 1. The level of HDL-C ($P < 0.001$), TCH/HDL-C ($P = 0.011$), LDL/HDL ($P = 0.015$) and HbA1C ($P = 0.053$) in both groups of men and women with diabetes were significantly different. Nevertheless, there was no statistically significant

Table1. The relationship between lipid factors and HbA1c amongst men and women

Variables	Sex		Total (Mean ± SD)	T-Test				
	Male (Mean ± SD)	Female (Mean ± SD)		t	p-value	Mean Difference	95% CI of the Difference	
							Lower	Upper
HbA1C	9.4 ± 1.8	9.1 ± 1.5	9.2 ± 1.7	1.9	.053*	.5	-.1	.9
Age (years)	58.1 ± 11.8	56.1 ± 9.9	57.1 ± 11.1	1.3	0.17	2.1	-.9	5.1
FBS(mg/dl)	184.9 ± 70.8	179.3 ± 67.5	182.2 ± 69.2	0.6	.55	5.6	-13.3	24.5
TCH(mg/dl)	176.4 ± 42.9	184.9 ± 41.8	180.4 ± 42.5	-1.4	.15	-8.4	-20.1	3.1
TG(mg/dl)	183.2 ± 117.0	183.1 ± 82.6	183.2 ± 101.8	.01	.99	.2	-27.7	28.1
HDL-C(mg/dl)	47.1 ± 9.8	52.5 ± 10.1	49.6 ± 10.3	-3.9	<.001***	-5.3	-8.1	-2.6
LDL-C(mg/dl)	94.2 ± 27.6	97.8 ± 26.9	95.9 ± 27.3	-.9	.34	-3.6	-11.1	3.8
Risk Ratio	3.5± .5	3.8 ± 0.6	3.6 ± .6	-2.5	.011**	-.2	-.4	-.1
AIP	.52 ± .39	.55 ± .21	.54 ± .32	-.7	.45	-.03	-.12	.05
LDL/HDL	2.1 ± 0.4	1.8 ± 0.4	1.9 ± .41	2.5	.015**	.1	.1	.3

Significant with *p<0.1, **p<0.05, ***p<0.01

difference in mean age, cholesterol, triglyceride, FBS, LDL-C and AIP between men and women (P> 0.05).

The relationship between HbA1C and lipid profiles demonstrates that among lipid factors, cholesterol level (p = 0.005) is directly correlated with HbA1C. Moreover, there was a direct correlation between LDL-C (p <0.001), LDL-C/HDL-C (p <0.001), and FBS (p <0.001) with HbA1C. However, there was no direct significant correlation between triglyceride, HDL, AIP, and risk ratio with HbA1c (P> 0/05) (Table 2).

Table2. Association of HbA1C with lipid factors.

	HbA1C	
	Pearson-Correlation	p-value
FBS(mg/dl)	.77*	<.001**
TCH(mg/dl)	.19*	.005**
TG(mg/dl)	.08	.22
HDL-C(mg/dl)	.05	.52
LDL-C(mg/dl)	.22*	.001**
Risk Ratio	.03	.68
AIP	-.12	.06
LDL-C/HDL-C	.24*	<.001**

*Correlation is significant at .01

Discussion

T2DM is a fundamental dilemma all over the world and is strongly associated with obesity. Due to hyperglycemia and insulin resistance syndrome.Moreover, patients with T2DM encounter a high risk for development of a wide range of microvascular disorders including neuropathy, retinopathy, and nephropathy as well as macrovascular problems affecting the cardiovascular system. T2DM is a multifactorial disorder with an etiological basis of environmental and genetic factors. Main complications resulted by T2DM include insulin resistance and complications of insulin secretion. In spite of this, there are other pathophysiological abnormalities that lead to deregulated metabolism of glucose(15).

In patients with T2DM, low levels of HDL-C and high levels of triglycerides and LDL-C are observed. In fact, this profile characterizes patients with insulin resistance syndrome, a case demonstrated in most patients with diabetes. Moreover, individuals who are prone to diabetes are reported with high levels of cholesterol, triglycerides, LDL-C, and low levels of HDL-C(4).

In this study, the correlation of HbA1c and hyperlipidemia was analyzed in T2DM patients. Our findings show a significant correlation between HbA1C levels and lipid factors including TCH, LDL-C, and LDL-C/HDL-C. However, there was no

significant correlation between HbA1C and HDL-C, TG, risk ratio and AIP. There was a significant difference between TCH/HDL-C, HDL-C, LDL-C/HDL-C and HbA1C in men and women. HDL-C and TCH/HDL-C levels were significantly higher in women than in men, and LDL-C/HDL-C and HbA1c levels were significantly higher in men. However, Wechsler(16) reported that the levels of TC and LDL-C were higher in women than men. This study showed that high occurrence of dyslipidemia could be a warning sign for cardiovascular disease. There was also a significant relationship between TC, and LDL-C with HbA1c. In several studies on patients with diabetes, a positive correlation was observed between HbA1c and TC, LDL-C, and TG(17, 18). Similarly, the association between HbA1c and FBG was similar to that in previous studies(19). Considering the results obtained in this study, it is suggested that HbA1c might be an indicator of long-term glucose control, and due to being directly correlated with lipid-like risk factors such as TCH, LDL-C and LDL/HDL, it might serve as a risk factor for cardiovascular disease as well as an index of increased levels of lipid factors in diabetic patients. Notwithstanding, there was no significant correlation found between AIP and risk ratio. Therefore, further research is needed to clarify the accuracy of this hypothesis.

The results of the current study are consistent with the results reported by Smatha et al in India. who examined the association between HbA1c and lipid profiles in patients with diabetes. Cases with an HbA1C level of >7% indicated a direct and significant correlation between this factor and TCH, LDL-C, and LDL-C/HDL-C. However, no difference in the levels of TG and HDL-C was observed between the two groups(20).

The study of Arshad et al. on patients with diabetes mellitus in Afghanistan showed a positive correlation between HbA1c and cholesterol, TG, LDL-C and LDL-C / HDL-C. However, no correlation was found between HDL-C and HbA1c. No significant change in the levels of TG, HDL-C, TCH, LDL-C and TCH/HDL-C was observed between the two groups(21). The results of our study are similar to the results reported by Arshad et al. In spite of this, a significant difference was observed in the levels of HDL-C and TCH/ HDL-C between the two groups in our study. This inconsistency might be due to the small sample size analyzed in our study.

In another study by Rajul and colleagues in 2016, the association between HbA1C and lipid profiles was evaluated. The levels of cholesterol, TG, HDL-C, LDL-C, and HbA1C were significantly higher in patients compared to controls. Furthermore, HbA1C was positively correlated with cholesterol, TG, LDL-C and negatively correlated with HDL-C(22). The contradictory results in our studies are likely due to low sample size and needs to be further investigated on a larger sample size.

Our results are consistent with the results of the following studies; Bodhe et al. performed a study on HbA1c as a predictor of dyslipidemia and atherogenicity in diabetes mellitus in India. They reported a direct correlation between HbA1C and TG, LDL-C, and AIP. No correlation was observed between HbA1C with TCH and HDL-C(23). In another study by Abedian on patients affected with diabetes, TG levels were higher in men and HDL-C levels were higher in women. HbA1c was directly correlated with LDL-C, AIP, TG, TCH and risk ratio, but not correlated with age, HDL-C/LDL-C and HDL-C(24). Although the findings of our study are similar to those reported by these studies, our results on AIP and HDL-C show inconsistency compared to the results of these studies. Since both studies were performed on a small sample size, further research on a larger sample size is required.

The study of Khan H.A et al in 2006 in India revealed a direct correlation between HbA1C and cholesterol, TG, and LDL, as well as an inverse correlation with HDL-C. Our results were consistent except for TG. Considering the sample size, the results of TG are more reliable(25).

Based on our results as well as the findings of other studies, there was a correlation between HbA1C and cardiovascular risk factors such as TCH, LDL-C, and LDL/HDL. Besides being a potential risk factor in cardiovascular disease, HbA1c could be used as a long-term indicator of blood glucose. However, further research is required to elucidate the status of risk ratio and AIP regarding the contradictory findings. This study is advantageous because little data is available and few studies were dedicated to the analysis of risk

ratio and AIP. In addition, the results of the risk ratio and AIP in our study are in contradiction with the results of previous studies. Moreover, our study presents highly reliable data. However, it is limited by small sample size and lack of personal information on whether individuals have consumed drugs. Further studies on larger samples with available medical records and medication outcome on people with diabetes are required in order to obtain more accurate and complete information on HbA1C and lipid profiles as well as its correlation with cardiovascular complications.

Acknowledgments

The authors would like to express their thanks to the student research committee of Mazandaran University of Medical Sciences for supporting this student research proposal with the code 253 (IR.MAZUMS.REC.1397.S253) adopted on February 23, 2018 and the cooperation of staff working at Bouali Hospital of Sari.

Conflict of interest

There is no conflict of interest among authors.

References

1. Association AD. Standards of Medical Care in Diabetes—2014. Diabetes Care 2014; 37 (Suppl. 1): S14–S80Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2014; 37 (Suppl. 1): S81–S90. Diabetes care. 2014;37(3):887-.

2. Hasan Z, Zia S, Maracy M. Baseline disease knowledge assessment in patients with type 2 diabetes in a rural area of northwest of Pakistan. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 2004;54(2):67-72.

3. Rani HS, Madhavi G, Rao VR, Sahay B, Jyothy A. Risk factors for coronary heart disease in type II diabetes mellitus. Indian journal of clinical biochemistry. 2005;20(2):75-80.

4. Ebrahimi-Far M, Mazdapour M, Kaki A, Mohammadi P, Zakerjafari M, Lavi A ea. Comparison of Biochemical Factors and Liver Enzymes in type 2 Diabetes Patients and Healthy Individuals. . Bull EnvPharmacol Life Sci. 2015;4(01-4).

5. Federation I. International Diabetes Federation: IDF Diabetes Atlas. Brussels, Belgium. 2013.

6. Gallagher EJ, Le Roith D, Bloomgarden Z. Review of hemoglobin A1c in the management of diabetes. Journal of diabetes. 2009;1(1):9-17.

7. Hasanvand B, Karami K, Khodadi A, Valipour M. Impact determination of strength and resistance training on Glycoside hemoglobin and blood sugar on patients with type II diabetes". Yafteh. 2011;13(3):75-81.

8. Karamati M, Sadeghyan M, Parezadeh M, F M. Relation between glycolyted hemoglobin and blood cholesterol in patient with type II diabete. Medical Journal of Mashhad University of Medical Sciences. 2008;5(3):159-64.

9. Kennel WB, DL M. Diabetes and cardiovascular disease: the framingham study. JAMA 1979.241:2035-8.

10. Carmena R. High risk of lipoprotein dysfunction in type 2 diabetes mellitus. Revista Española de Cardiología. 2008;8(Supl. C):18-24.

11. Stratton IM, Adler AI, Neil HAW, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. Bmj. 2000;321(7258):405-12.

12. Robinson D, Luthra M, Vallis M. Canadian diabetes association clinical practice guidelines expert committee. Canadian diabetes association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes. 2013;37(suppl 1):S1-S212.

13. SALEHIN S, AZIZIMOGHADAM A, AMIRSHAHI M, ABDOLLAHIMOHAMMAD A. A STUDY ON CORRELATION BETWEEN GLYCOSYLATED HEMOGLOBIN, BODY MASS INDEX, DISEASE DURARUION, INSULIN DOSAGE AND MENSTRUAL DURATION IN TYPE 1 DIABETIC ADOLESCENTS. 2013.

14. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus.. Nat Rev Dis Primers. 2015;1(15019).

15. Wexler DJ, Grant RW, Meigs JB, Nathan DM, Cagliero E. Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes. Diabetes care. 2005;28(3):514-20.

16. Erciyas F, Taneli F, Arslan B, Uslu Y. Glycemic control, oxidative stress, and lipid profile in children with type 1 diabetes mellitus. Archives of medical Research. 2004;35(2):134-40.

17. Dr. Haider Mohammed Fayyad Alyasiri, Dr.AliAbidSadoon, Dr.KadhimMohan. RELATIONSHIPBETWEENHBA1CAND HYPERLIPIDAEMIAINPATIENTSWITH DIABETESMELLITUS. Thi-QarMedicalJournal(TQMJ). 2012;6(1):67-71.

18. Rosediani M, Azidah A, Mafauzy M. Correlation between fasting plasma glucose, post prandial glucose and glycated haemoglobin and fructosamine. The Medical journal of Malaysia. 2006;61(1):67-71.

19. Samatha P, Prabodh V, Chowdary N, Shekhar R. Glycated hemoglobin and serum lipid profile associations in type 2 diabetes mellitus patients. J Pharmac Biomed Sci. 2012;17(17):1-4.

20. Hussain A, Ali I, Ijaz M, Rahim A. Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: hemoglobin A1c prognosticates dyslipidemia. Therapeutic advances in endocrinology and metabolism. 2017;8(4):51-7.

21. Dr.RajulLodha, Dr.Renuka Z Lal, Dr.ShwetaBiyani. HbA1c as screening biomarker of dyslipidemia in Type 2 Diabetes mellitus patients. Sch J App Med Sci. 2016;4(5C):1600-2.

22. Bodhe C, Jankar D, Bhutada T, Patwardhan M, Patwardhan V. HbA1c: predictor of dyslipidemia and atherogenicity in diabetes mellitus. International Journal of Basic Medical Sciences and Pharmacy (IJBMSP). 2012;2(1).

23. Parsanasab H, Moradi Pudeh B, Alizadeh A, Abediankenari S. Evaluation of correlation between HbA1c with the Risk factors of lipid profile in patients with type 2 diabetes. Journal of Mazandaran

University of Medical Sciences. 2013;22(2):153-6.
24. Khan H, Sobki S, Khan S. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA 1c predicts dyslipidaemia. Clinical and experimental medicine. 2007;7(1):24-9.