ORIGINAL RESEARCH

Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study

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Background: To investigate the association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus (T2DM) at a tertiary care hospital in Jeddah, Saudi Arabia (SA).

Methods: The present retrospective cross-sectional study was accomplished at the Faculty of Medicine, King Abdulaziz University (KAU), Jeddah, SA, between April and July 2018. There were 206 T2DM patients selected for the study (141 females and 65 males), and the data were collected through a review of the electronic profiles of patients by using the medical electronic file system used at the KAU Hospital. Biochemical data such as fasting plasma glucose (FPG), HbA1c and lipid profile, along with the patient's age, BMI and gender, were also taken from the electronic file system. The inclusion criteria allowed for only patients who were regularly seeing their physician and whose electronic file was up to date.

Results: The participants' data were analyzed gender-wise. The females had significantly higher values for BMI (p=0.002), HbA1c (p=0.009), triglycerides (TGs) (p<0.001), high-density lipoprotein cholesterol (HDL-C) (p=0.002) and low-density lipoprotein cholesterol (LDL-C) (p<0.001) compared to the males. The study subjects were grouped according to their level of HbA1c (good glycemic index <7%, and poor glycemic index >7%). In both groups, no significant differences were found in any of the parameters other than TGs (p=0.020) and HbA1c (p<0.001). An analysis of the correlation between HbA1c and other parameters exhibited a significant correlation with TG (r=0.16, p=0.020), while no significant relationship was observed with the other variables. The linear regression results indicated that HbA1c values were associated with TGs (p=0.020) and were independent of age, BMI, TC, LDL-C, HDL-C and FPG levels.

Conclusion: The glycated Hb was associated with TGs, and no significant association was found with age, BMI, TC, LDL-C, HDL-C and FPG levels.

Keywords: glycated hemoglobin, DMT2, glycemic control, dyslipidemia, lipid profile

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Introduction

Globally, type 2 diabetes mellitus (T2DM) is a swiftly escalating public health issue with noteworthy effects on human health, living standards, the economy and health care systems.[1] Statistics from the International Diabetes Federation (IDF) indicate that 425 million adults worldwide have diabetes mellitus (DM) and that by 2045, the number of DM patients will be 629 million and 352 million people were at risk of developing T2DM.[2]

T2DM patients are prone to diabetic dyslipidemia, which puts them at risk of developing macrovascular (stroke, peripheral vascular disease and coronary artery disease [CAD]) and microvascular (nephropathy, neuropathy and retinopathy) diseases.[3] Naqvi et al (2017) have reported that, for T2DM patients, one of the most common complications linked with uncontrolled hyperglycemia is dyslipidemia.[4]

Glycated hemoglobin (HbA1c) levels are routinely measured in diabetics to monitor their glycemic control. The goal is to achieve a level below 7%. Levels of HbA1c can be affected by multiple factors, including sugar intake, exercise and adherence to medications. Some studies have reported that HbA1c could potentially be utilized as a possible biomarker for predicting dyslipidemia and cardiovascular disease (CVD).[5,6]

The level of circulating HbA1c is taken as the gold standard of glycemic control, and regulating it is imperative for avoiding T2DM complications. HbA1c values not only reflect glycemic control but are also the main factor in determining the risk of diabetes-related complications[7] and mortality.[8]

There are several conflicting results in the literature, such as a Turkish study that found a significant relationship between total cholesterol (TC), LDL, triglycerides (TGs) and HbA1c,[9] while others reported no considerable relationship.[10] Similarly, while one study reported a significant negative relationship between HbA1c and LDL-C,[11] others reported the opposite results.[6] Importantly, a recent study revealed a positive relationship between HbA1c and high TGs, concluding that HbA1c could be a sign of TG levels and that it may predict CVD risk factors in T2DM.[4]

These reports indicate there is a discrepancy regarding the relationship between HbA1c and the lipid profile. Further studies could determine more precisely the relative risks of developing dyslipidemia that are dependent on HbA1c levels in order to truly say whether it is a marker for dyslipidemia in diabetics. Our study investigated the association between HbA1c and the lipid profile in patients with T2DM in a tertiary care hospital in Jeddah, Saudi Arabia (SA).

Materials and methods

The present retrospective cross-sectional study was accomplished at the Faculty of Medicine at the King Abdulaziz University Hospital (KAUH) in Jeddah, SA, and the protocol was approved by the Research Ethics Committee (REC) of King Abdulaziz University, Jeddah, SA (Reference No. 15-18-03). A written informed consent was obtained and documented from all participants, covering the study and publication of results, and they were informed about the nature of the study and the confidentiality of the study subjects was maintained. Moreover, this study was conducted in accordance with the Declaration of Helsinki.

The data were collected by reviewing the electronic profiles of the participating patients, using the medical electronic file system in place at KAUH. Biochemical data such as FPG, HbA1c, and lipid profile, along with age and gender, were also taken from the electronic file system. Moreover, patients were only selected for the study if they were seeing their physicians regularly and their data was up-to-date in the system.

Patients with an established diagnosis of T2DM were selected according to the American Diabetes Association criteria established in 2007. These criteria set the following as values that are indicative of T2DM: HbA1C ≥6.5%, FPG ≥126 mg/dl (7.0 mmol/l), 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT), or random plasma glucose ≥200 mg/dl (11.1 mmol/l).[12]

Patients suffering from CVD, thyroid disorders, renal problems and other endocrinopathies and those taking lipid-lowering agents were excluded from the study, as was one patient who had type 1 diabetes. The patients were selected from both genders who presented to the outpatient department of KAUH between April 2018 and July 2018. There were 206 patients who met our eligibility criteria, and their histories and examination data regarding their T2DM presenting symptoms, complications, treatment modalities, smoking and social drugs consumption and any other addictions were noted. OpenEpi version 3 was used to calculate the sample size $n=[DEFF*Np(1-p)]/[(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$; the prevalence of the problem was taken at 62.5%[13] and the confidence level at 80%. The calculated sample size was 154.

All patients' anthropometric measurements (weight, height and BMI), blood pressure and laboratory results, including HbA1c levels, TC levels, TG levels, LDL-C levels and HDL-C levels, were collected. For all DM patients, blood samples were collected between 8:00 and 10:00 AM (12–14 h fasting), and plasma was used for estimating the glucose level. The FPG, and HbA1c and lipid profile levels were determined by using an autoanalyzer (Roche Modular P-800, Roche Diagnostics, Germany). For analysis, we characterized the

participants' glycemic control as poor (HbA1c >7%) or good (HbA1c <7%).[5]

SPSS version 21 (IBM Corp., Armonk, NY, USA) was employed to compute the data. A Shapiro–Wilk test confirmed that the data were normally distributed. Therefore, the Student's *t*-test was used for comparison, and quantitative data were stated as the mean and standard deviation. The Pearson correlation coefficient was applied to measure the correlation between various parameters, and an independent sample *t*-test was utilized to measure the mean difference between different parameters. A linear regression test was computed to find out the association between HbA1c and lipid profile, FPG, BMI and age; the results were regarded as non-significant when the *p*-value was >0.050.

Results

A total of 206 T2DM patients were selected for the study (141 females and 65 males). The participants' basic characteristics were analyzed and compared according to gender (Table 1). The females had significantly higher values for BMI (*p*=0.002), TC (*p*<0.001), HDL-C (*p*=0.002), LDL-C (*p*<0.001) and HbA1c (*p*=0.009) compared to the males, while the age of the males was, on average, significantly higher than the females (*p*<0.001).

There were 90 (43.69%) patients in the group with HbA1c levels <7%, and 116 (56.31%) subjects in the group with HbA1c levels >7%. There was no significant difference in any parameter except for TG level (*p*=0.020) and HbA1c (*p*<0.001) (Table 2).

Table 3 shows the Pearson correlation of HbA1c with other variables. A significant correlation of HbA1c was observed with TG (*r*=0.16, *p*=0.02) but there were no significant correlations with the other parameters.

The results from a linear regression analysis indicated that the HbA1c values were associated with TG (*p*=0.020)

and were independent of age, BMI, TC, LDL-C, HDL-C and FPG levels (Table 3).

Discussion

HbA1c levels could be employed as a possible biomarker for recognizing T2DM patients at risk of CVD and could be used as a guide for treating patients.[4,14] Our results display a significant positive relationship between HbA1c and TG. A similar correlation has been reported by several other studies[1,9] that found a positive relationship between HbA1c and high TG levels, in agreement with the present study, although one other study reported no correlation between HbA1c and TG.[10]

The findings of this study and the others mentioned above indicates that HbA1c is a direct indicator of increased TG and indirectly helps in assessing the risk for macro- and microvascular problems.[1,4]

In T2DM subjects, insulin resistance is considered the cause of dyslipidemia. The reasons for increased TG levels in T2DM patients is an inadequate secretion or function of insulin that causes enhanced hepatic secretion of very low-density lipoprotein (VLDL) along with the late removal of TG-rich lipoproteins, mainly due to enhanced substrate levels for TG synthesis.[15]

The present study found no relationship between HbA1c and TC or LDL-C. Our results are consistent with another study also reporting no significant relationship between these parameters.[10] However, these results are inconsistent with the results of numerous other studies that have stated a significant relationship between HbA1c and TC and LDL-C.[1,3,14]

Further, our results show a statistically non-significant negative link between HbA1c and HDL-C. This is in agreement with the results from a few other studies[1,9] but is inconsistent with several studies that reported a notable

Table 1 Gender-wise comparison of basic characteristics of type 2 diabetes mellitus patients

Parameters	Mean ± SD Total (N=206)	Mean ± SD Females (N=141)	Mean ± SD Males (N=65)	*p*-value
Age (yrs)	60.46±13.54	58.53±14.19	64.66±10.99	<0.001*
BMI (Kg/m²)	30.8±6.1	31.59±6.56	29.08±4.58	0.002*
HbA1C (%)	7.65±1.78	7.86±1.86	7.20±1.53	0.009*
Total cholesterol (mg/dl)	170.14±40.9	174.40±39.8	152.35±40.2	<0.001*
HDL-C (mg/dl)	47.56±16.2	49.88±17.01	42.53±13.14	0.002*
LDL-C (mg/dl)	103.24±36.3	109.43±36.34	89.32±31.70	<0.001*
Triglyceride (mg/dl)	143.48±86.8	140.82±77.94	148.79±103.6	0.57
FPG (mg/dl)	147.78±58.7	142.38±51.66	159.3±58.88	0.07

Note: *Significant *p*-value.
Abbreviations: BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; FPG, Fasting plasma glucose.

Table 2 Comparison of basic characteristics of type 2 diabetes mellitus patients according to their glycemic control

Parameter	Good glycemic control (HbA1C level <7%) (N=90)	Poor glycemic control (HbA1C ≥7%) (N=116)	p-value
	Mean ± SD	Mean ± SD	
Age (yrs)	61.6±13.13	59.58±13.85	0.29
BMI (Kg/m^2)	30.10±5.45	31.34±6.54	0.139
HbA1C (%)	6.13±0.60	8.84±1.47	<0.001
Total cholesterol (mg/dl)	162.80±37.89	170.92±43.31	0.154
HDL-C (mg/dl)	49.49±17.78	46.40±15.08	0.20
LDL-C (mg/dl)	99.38±37.89	105.95±34.41	0.21
Triglyceride (mg/dl)	128.42±70.85	154.11±96.65	0.02*
FPG (mg/dl)	144.36±56.88	152.28±55.44	0.32

Note: *Significant p-value.
Abbreviations: BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; FPG, Fasting plasma glucose.

Table 3 Correlation analysis (between HbA1C and age, BMI, FBS, and lipid parameters) and linear regression analysis of T2DM patients showing dependency of HbA1C on other variables

Parameter	Correlation		Regression analysis	
	Coefficient	p-value	Unstandardized Coefficients b	p-value
Age (yrs)	−0.066	0.346	−0.049	0.56
BMI (Kg/m^2)	0.035	0.614	0.00	0.63
Total cholesterol (mg/dl)	0.132	0.06	0.133	0.47
HDL-C (mg/dl)	−0.084	0.232	−0.113	0.12
LDL-C (mg/dl)	0.093	0.186	−0.553	0.54
Triglyceride (mg/dl)	0.164	0.02*	0.351	0.02*
FPG (mg/dl)	−0.092	0.191	−0.052	0.40

Note: *Significant p-value.
Abbreviations: BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; FPG, Fasting plasma glucose.

negative relationship between HbA1c and HDL-C.[10,11,14] Few other studies have described a positive relationship between HbA1c and HDL-C.[6,16] Our results could be explained by the fact that among our female group, there were significantly higher levels of HbA1c (Table 1) compared to the male group and by the fact that females typically have higher HDL-C levels compared to males. Therefore, no significant negative correlation was found.

The linear regression analysis revealed the link between HbA1c values and TGs (p=0.020) and further showed that the correlation is independent of age, BMI, TC, LDL-C, HDL-C and FPG levels. Hussain et al (2017) also reported that HbA1c could be a predictor of TG, TC and LDL-C.[1]

The gender-wise comparison showed that the females had significantly higher values for BMI, TC, LDL-C, HDL-C and HbA1c as compared to the males. Again, a few other studies have reported similar results.[6,17] However, in this case, our results are dissimilar in some

ways to those other studies.[5,18] One of the reasons for the gender-wise difference in lipid parameters could be the influence of sex hormones on the distribution of body fat that causes altered lipoprotein levels.[19] The difference in our results could also be due to the differences in BMIs and ages between the two groups as well as the length of time since diagnosis with DM. Our subjects had a mean BMI >30, which means they were obese. Firouzi et al (2015) reported the association of obesity and physical inactivity with poor blood sugar control.[20]

The present study found that the subjects with HbA1c levels above 7% (poor glycemic control) had significantly higher TG levels compared to the group with HbA1c <7% (good glycemic control); however, no significant variance was found in the other parameters. Another study reported similar results,[6] and a few studies had results displaying significantly elevated levels of TC, LDL-C and TGs along with reduced HDL-C in subjects with HbA1c over 7% compared to those subjects with HbA1c <7%.[5,6] It seems

that patients with good glycemic control have less dyslipidemia compared to patients with poor glycemic control.

A recent study in Pakistan has concluded that the trend of the complexity of CAD increases with age, high HbA1c, high LDL-C, increased TGs and decreased HDL-C levels.[21] Hussain et al, (2017) reported that HbA1c is not only a dependable glycemic index but also a forecaster of dyslipidemia.[1] Each 1% change in HbA1c values above the normal level shows a variation of approximately 35 mg/dl in the mean blood glucose level.[22,23] Importantly, a 1% drop in the HbA1c level decreases the 40% risk of microvascular complications.[23] However, the literature indicates the positive effects of enhanced physical activity and lifestyle modifications in improving glycemic control and dyslipidemia.[24]

It is suggested that diabetes patients should join a fitness program and do regular exercise that comprises 30 mins of mild-intensity physical activity 4–6 times per week, with a minimum outlay of 200 Kcal.[25] It is also suggested that every family physician be well aware of the relationship between HbA1c and hyperlipidemia in T2DM patients and check their patients' lipid profile and HbA1c at least twice a year to avoid future problems.

The differences we found in our study in SA compared to studies from other parts of the world regarding the relationship between HbA1c, and lipid profile parameters might be attributable to the difference in population, as the prevalence of dyslipidemia in SA is already high, even in non-diabetics.[26]

The patients included in our study were all taking different antidiabetic medications. However, we could not analyze the data according to the treatment modalities, and it is possible that such a patient grouping would have some impact on the study results.

The strength of the study is that we had the complete biochemical data of the patients and we computed a comparison, a correlation and a regression analysis. The present study had a few limitations, including being a retrospective study as well as having too small of a sample size and the fact that patients' dietary habits, lifestyle patterns, time since diagnosis with DM and duration of regular physical activity were undetermined.

Conclusion

HbA1c was associated with TGs, while no significant associations were found with age, BMI, TC, LDL-C, HDL-C or FPG levels.

Therefore, the use of HbA1c as a sign of dyslipidemia in our population should be undertaken with caution. We recommend longitudinal and case-controlled studies to be conducted in this region to explore the link between glycemic control and lipid profiles. There is a need for an educational program for diabetic patients regarding blood sugar control and the deleterious consequences of dyslipidemia. Awareness of this risk among family physicians and T2DM patients can play a pivotal role in controlling and avoiding the grave consequences of this complication for T2DM patients.

Consent

The authors confirm that all patients provided informed consent forms.

Data sharing statement

All original data is available in the Department of Family Medicine, King Abdulaziz University, Jeddah, SA. The data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgments

Author contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

Financial support was received from King Abdulaziz University (DSR), Jeddah, under grant No. (D-063-140-1440). The authors report no other conflicts of interest in this work.

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