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ORIGINAL ARTICLE

Clinical significance of HbA_{1c} as a marker of circulating lipids in male and female type 2 diabetic patients

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Abstract Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular deaths. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality. Glycated hemoglobin (HbA_{1c}) is a routinely used marker for long-term glycemic control. This investigation is an attempt to evaluate the diagnostic value of HbA_{1c} in predicting diabetic dyslipidemia. Venous blood samples were collected from 2,220 type 2 diabetic patients (ages, 35–91 years; male/female ratio, 1.07). The sera were analyzed for HbA_{1c}, fasting blood glucose (FBG), total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL). The levels of HbA_{1c} did not differ significantly between males (8.33 ± 0.06%) and females (8.47 ± 0.07%), whereas female patients had significantly higher FBG (10.01 ± 0.13 mmol/l) than males (9.31 ± 0.11 mmol/l). HbA_{1c} showed direct and significant correlations with cholesterol, triglycerides and LDL and inverse correlation with HDL. Female diabetic patients had significantly higher levels of serum cholesterol (5.42 ± 0.03 vs. 5.18 ± 0.03 mmol/l) and HDL (1.32 ± 0.01 vs. 1.12 ± 0.01 mmol/l) as compared to males. There was no significant difference in triglycerides and LDL between the two genders. Older patients (>70 years) had significantly lower FBG, cholesterol, triglycerides and LDL. There was a linear and significant increase in triglycerides in the patients of both genders with impaired glycemic control. Both male and female patients with worse glycemic control ($HbA_{1c} > 9\%$) had significantly high cholesterol and LDL levels. Serum HDL showed a significant and inverse relationship with uncontrolled hyperglycemia in females but not in males. These findings clearly suggest that HbA_{1c} can provide valuable supplementary information about the extent of circulating lipids besides its primary role in monitoring long-term glycemic control. Further studies are warranted to reinforce the potential of HbA_{1c} as a biomarker for screening of high-risk diabetic patients.

Keywords Type 2 diabetes · Dyslipidemia · Glycemic control · HbA_{1c} · Serum lipids · Biomarker

Introduction

Diabetes is a global endemic with rapidly increasing prevalence in both developing and developed countries [1]. There is a high risk of cardiovascular disease (CVD) in people with type 2 diabetes, while cardiovascular deaths represent the top killer in this population [2]. Hyperglycemia is the apparent feature of diabetes due to diagnostic dependency of patients on blood glucose measurements. However, most of the individuals may also carry unnoticed dyslipidemia, characterized by increased levels of triglycerides and LDL and decreased HDL. Individuals with coexisting diabetes and metabolic syndrome (dyslipidemia + hyperglycemia + hypertension) have the highest prevalence of CVD [3]. Giansanti et al. [4] also observed significantly higher levels of hypercholesterolemia and hyperlipidemia in type 2 diabetic patients with CVD as compared to diabetic patients without CVD. Early therapeutic interventions, aiming to reduce triglycerides and LDL and to increase HDL, significantly reduce cardiovascular events and mortality in patients with type 2 diabetes [5, 6].

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A significant correlation between dyslipidemia and systolic blood pressure has been observed in type 2 diabetics, suggesting their increased susceptibility to vascular disease associated with LDL [7]. It is likely that the combination of hyperglycemia, diabetic dyslipidemia, insulin resistance and hypertension produces an enhanced atherogenic environment within the circulation [8]. Infiltration of lipoproteins in arterial wall and dermal tissue has been implicated in atherosclerosis and xanthoma, respectively. Severe hyperlipidemia in diabetes may also lead to lipid infiltration into the retina, causing macular edema and retinal hard exudates [9] and blindness [10].

The Diabetes Complications and Control Trial (DCCT) established glycosylated hemoglobin (HbA_{1c}) as the gold standard of glycemic control, with levels ≤7% deemed appropriate for reducing the risk of vascular complications [11]. Elevated HbA_{1c} has been regarded as an independent risk factor for coronary heart disease (CHD) [12] and stroke [13] in subjects with or without diabetes. Ravipati et al. [14] observed a direct correlation between HbA_{1c} and the severity of coronary artery disease (CAD) in diabetic patients. Whereas, improving the glycemic control can substantially reduce the risk of cardiovascular events in diabetics [15, 16]. Moreover, attempts to reduce cardiovascular risks resulted in the improvement of HbA_{1c} even in the absence of any specific intervention targeted at improving glycemic control [17]. Nakamura et al. [18] have observed significant elevation of soluble form of receptor for advanced glycation end products (sRAGE) in type 2 diabetic patients with CAD. They also demonstrated significant association between sRAGE and HbA_{1c} as well as serum lipids [18].

In view of above literature, it was rationalized to testify the potential of HbA_{1c} as a possible predictor of dyslipidemia in type 2 diabetes. We, therefore, examined the relationship between glycemic control and serum lipid profile and evaluated the relevance of HbA_{1c} as an indicator of circulating lipids in type 2 diabetic patients.

Patients and methods

This retrospective study comprised a total of 2,220 type 2 diabetic patients who visited the clinics of Armed Forces Hospital, Riyadh. There were 1,148 males and 1,072 females. The mean age ± standard deviation of male and female subjects were 59.93 ± 9.72 years and 57.46 ± 11.15 years, respectively. The age of male patients ranged between 36 and 91 years and of female patients ranged between 35 and 91 years. All the patients were categorized into four age groups: ≤50 years (534 patients), >50–60 years (772 patients), >60–70 years (619 patients) and >70 years (295 patients).

Venous blood samples from all the subjects were collected in serum separator tubes after at least 8 h fasting. The sera were analyzed for glycated hemoglobin (HbA_{1c}), fasting blood glucose (FBG), total cholesterol, triglycerides (TG) and high-density lipoprotein cholesterol (HDL) using an autoanalyzer (Roche Modular P-800, Germany). The level of low-density lipoprotein cholesterol (LDL) was determined using the formula: LDL = (cholesterol—TG)/(2.2 HDL). The impact of glycemic control on various parameters was evaluated by categorizing all the patients into three categories on the basis of HbA_{1c} levels: $HbA_{1c} \leq 6\%$ (good glycemic control), $HbA_{1c} > 6$–9% (poor glycemic control) and $HbA_{1c} > 9\%$ (worse glycemic control). The selection of these cutoff values of HbA_{1c} was based on earlier studies [15, 18–21].

The data were analyzed by SPSS version 10. Pearson's correlation test was performed to examine various correlations. Independent samples Student's *t*-test (2-tailed) was used to compare the means of different parameters between males and females. One-way analysis of variance (ANOVA) and post-hoc Dunnett's multiple comparison tests were used to examine the significance levels for various biochemical parameters in age-categorized groups. Univariate analysis was performed to evaluate the effects of gender, age and glycemic control on serum lipid profile. *P* values ≤0.05 were considered as statistically significant.

Results

Both male and female diabetic patients exhibited similar patterns of glycemic control depending on three cutoff values of HbA_{1c} (Table 1). There was no significant correlation between patient age and HbA_{1c}, whereas a highly significant correlation was observed between FBG and HbA_{1c} (Fig. 1). HbA_{1c} also demonstrated direct and significant correlations with cholesterol, triglycerides and LDL and inverse correlation with HDL (Fig. 1).

The levels of HbA_{1c} were slightly higher (1.69%, not significant) and of FBG significantly higher (7.54%, $P < 0.001$) in females as compared to male patients (Table 2). Among the circulating lipids, total cholesterol and HDL were significantly higher in female patients. Although the levels of triglycerides were lower and of LDL higher in females than males, these differences were not statistically significant (Table 2).

Alterations in serum biochemical parameters in various age groups of patients are shown in Table 3. Older patients had significantly lower FBG (ANOVA $F = 2.33$, $P = 0.044$), cholesterol ($F = 11.52$, $P < 0.001$), triglycerides ($F = 3.04$, $P = 0.028$) and LDL ($F = 11.89$, $P < 0.001$). However, there was no significant difference between HbA_{1c} ($F = 1.77$, $P = 0.150$) as well as HDL

Table 1 Distribution of subjects according to gender and HbA_{1c} cutoffs

Glycemic control	HbA_{1c} criteria	Male		Female		Total subjects	
		Number	Percentage	Number	Percentage	Number	Percentage
Good	≤6%	157	13.67	142	13.25	299	13.47
Poor	>6–9%	617	53.75	533	49.72	1150	51.80
Worst	>9%	374	32.58	397	37.03	771	34.73
All subjects	–	1,148	100.00	1072	100.00	2220	100.00

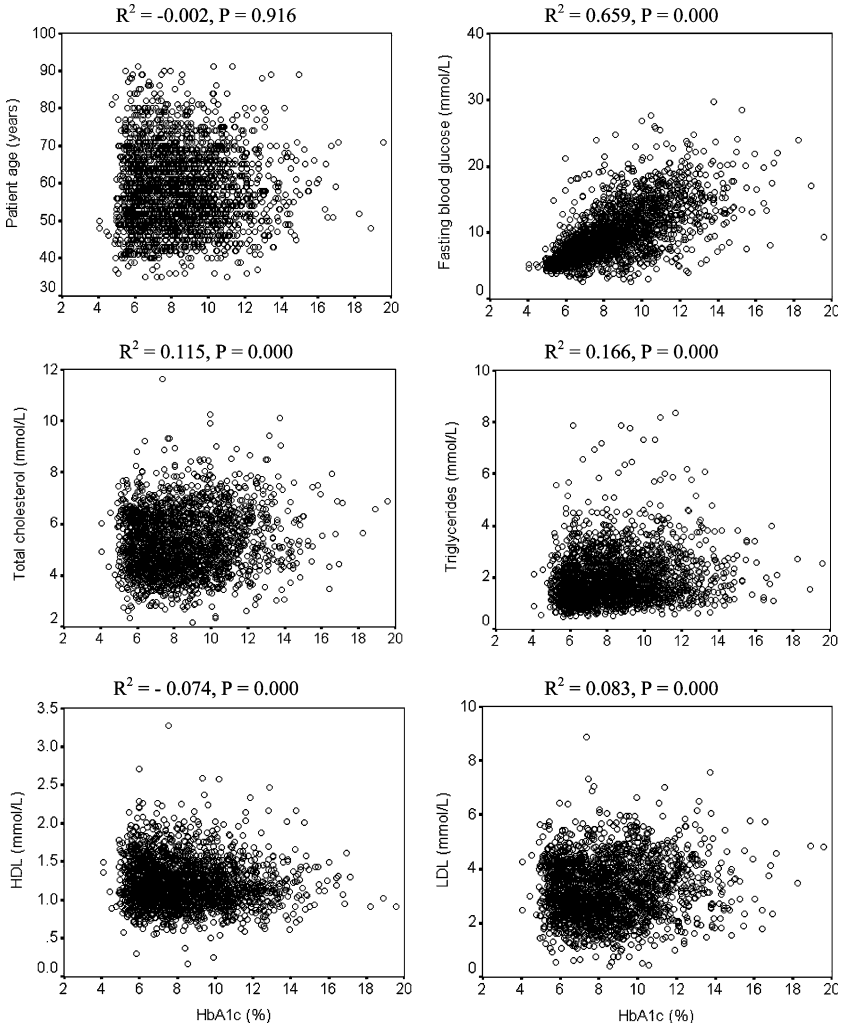

Fig. 1 Correlations between HbA_{1c} and age, fasting blood glucose (FBG) and serum lipid profile in type 2 diabetic patients

($F = 1.89$, $P = 0.128$) among the patients of different age groups (Table 3).

Diabetic patients with poor ($HbA_1 > 6$–9%) and worse ($HbA_{1c} > 9\%$) glycemic control had significantly higher levels of FBG (ANOVA $F = 591.52$, $P < 0.001$) and triglycerides ($F = 29.06$, $P < 0.001$) and significantly lower levels of HDL ($F = 8.57$, $P < 0.001$) as compared to patients with good glycemic control ($HbA_{1c} \leq 6\%$; Table 4). There was a significant increase in total cholesterol ($F = 18.45$, $P < 0.001$) and LDL ($F = 14.57$, $P < 0.001$) in diabetic patients with worse glycemic control as compared to the poor glycemic control group (Table 4).

The results of univariate analysis addressed the impact of patient gender, age and HbA_{1c} in predicting/influencing serum lipids (Table 5). Patients' gender was significantly associated with lipid parameters in decreasing magnitude in the following: HDL ($F = 184.69$) < cholesterol ($F = 11.93$) < triglycerides ($F = 3.77$). Patients' age demonstrated a significant association with LDL ($F = 10.99$), cholesterol

Table 2 Serum biochemistry categorized by patients' gender

Parameter	Gender of patients	
	Male (N = 1,148)	Female (N = 1,072)
HbA_{1c}	8.332 ± 0.066	8.473 ± 0.070
FBG	9.306 ± 0.111	10.008 ± 0.131*
Cholesterol	5.187 ± 0.035	5.421 ± 0.035*
Triglycerides	1.967 ± 0.029	1.909 ± 0.029
HDL	1.123 ± 0.007	1.317 ± 0.009*
LDL	3.172 ± 0.031	3.248 ± 0.032

All the values are in mmol/l except HbA_{1c}, which is reported as percentage

* $P < 0.001$ versus males (t-test)

(F = 9.55) and HDL (F = 2.99), but not with triglycerides (F = 1.50, P = 0.211). HbA_{1c} appeared to be a good predictor of triglycerides (F = 22.73) followed by cholesterol (F = 15.92), LDL (F = 12.73) and HDL (F = 9.64). There were no significant interactions for gender × HbA_{1c} and age × HbA_{1c} with respect to serum lipid profile (Table 5).

The comparative effects of glycemic control in male and female diabetic patients are shown in Fig. 2. Patients' age had no significant impact on glycemic control in both genders. There was a linear relationship between glycemic control and FBG, while both male and female patients with poor and worse glycemic control had significantly higher FBG as compared to patients with good glycemic control (Fig. 2). Female patients with good glycemic control had comparatively higher cholesterol, HDL and LDL as compared to males with the same level of glycemic control. Both male and female patients with worse glycemic control (HbA_{1c} > 9%) possessed significantly high cholesterol as compared to patients of respective gender and having poor glycemic control (Fig. 2). There was a linear and significant increase in triglycerides in the patients of both genders with impaired glycemic control. Both males and females with worse glycemic control had significantly high LDL levels. On the other hand, serum HDL showed a significant and inverse relationship with uncontrolled hyperglycemia in females, but not in males (Fig. 2).

Table 4 Serum biochemistry categorized by patients' glycemic control (HbA_{1c})

Parameter	HbA_{1c}		
	≤6% (N = 299)	>6–9% (N = 1,150)	>9% (N = 771)
FBG	5.958 ± 0.096	8.548 ± 0.083**	12.715 ± 0.153**#
Cholesterol	5.323 ± 0.063	5.163 ± 0.034	5.496 ± 0.045#
Triglycerides	1.659 ± 0.045	1.883 ± 0.027**	2.132 ± 0.040**#
HDL	1.277 ± 0.019	1.218 ± 0.008*	1.192 ± 0.010**
LDL	3.300 ± 0.055	3.093 ± 0.031*	3.347 ± 0.022#

All the values are in mmol/l

* $P < 0.05$ and ** $P < 0.001$ versus ≤ 6% group (Dunnett's test)

# $P < 0.001$ versus >6–9% group (Dunnett's test)

Discussion

The distribution of subjects according to gender and specific HbA_{1c} cutoffs showed that most of the type 2 diabetic patients experience poor or worse glycemic control irrespective of their gender (Table 1). A significant correlation between HbA_{1c} and FBG (Fig. 1) is in agreement with earlier reports [19, 22, 23]. We also observed significant correlations between HbA_{1c} and cholesterol, triglycerides, HDL and LDL in diabetic patients (Fig. 1). Several investigators have reported significant correlations between HbA_{1c} and lipid profiles and suggested the importance of glycemic control in normalizing dyslipidemia [23–26]. Although the levels of HbA_{1c} did not differ significantly between the two genders,

Table 3 Serum biochemistry categorized by patients' age

Parameter	Age of patients			
	≤50 years (N = 534)	51–60 years (N = 772)	61–70 years (N = 619)	>70 years (N = 295)
HbA_{1c}	8.275 ± 0.098	8.486 ± 0.084	8.484 ± 0.088	8.224 ± 0.128
FBG	9.778 ± 0.182	9.597 ± 0.145	9.840 ± 0.166	9.122 ± 0.209$
Cholesterol	5.464 ± 0.049	5.390 ± 0.042	5.147 ± 0.045*#	5.090 ± 0.075*#
Triglycerides	1.934 ± 0.043	2.006 ± 0.036	1.924 ± 0.040	1.805 ± 0.048#
HDL	1.221 ± 0.012	1.201 ± 0.010	1.219 ± 0.013	1.249 ± 0.019
LDL	3.368 ± 0.045	3.280 ± 0.038	3.068 ± 0.040*#	3.027 ± 0.066*#

All the values are in mmol/l except HbA_{1c}, which is reported as percentage

$ $P < 0.05$ versus 61–70 years group (Dunnett's test)

* $P < 0.001$ versus ≤50 years group (Dunnett's test)

# $P < 0.01$ versus 51–60 years group (Dunnett's test)

Table 5 Univariate analysis of variance model to evaluate the effects of gender, age, HbA_{1c} and their interactions on serum lipid profile

Source	*df*	Cholesterol		Triglycerides		HDL		LDL	
		F	*P*	*F*	*P*	*F*	*P*	*F*	*P*
Model	23	5.16	0.000	4.25	0.000	13.24	0.000	4.15	0.000
Sex	1	11.93	0.001	3.77	0.052	184.69	0.000	1.16	0.281
Age	3	9.55	0.000	1.50	0.211	2.99	0.030	10.99	0.000
HbA1c	2	15.92	0.000	22.73	0.000	9.64	0.000	12.73	0.000
Sex × HbA_{1c}	2	0.20	0.814	2.55	0.078	0.84	0.429	0.17	0.840
Age × HbA_{1c}	6	1.28	0.263	0.13	0.991	0.46	0.835	1.68	0.120

female patients showed significantly high levels of FBG (Table 2). Diabetes confers a markedly increased risk of cardiovascular events in both males and females [27]. However, women with diabetes are more susceptible to increased cardiovascular mortality [28]. Diabetic women may be subject to more adverse changes in coagulation, vascular function and cardiovascular risk factors than diabetic men [29–31]. The results of lipid profile showed that female diabetic patients had significantly higher levels of cholesterol and HDL, which is in agreement with earlier reports [32–35]. Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, leading to differences in altered lipoproteins [36].

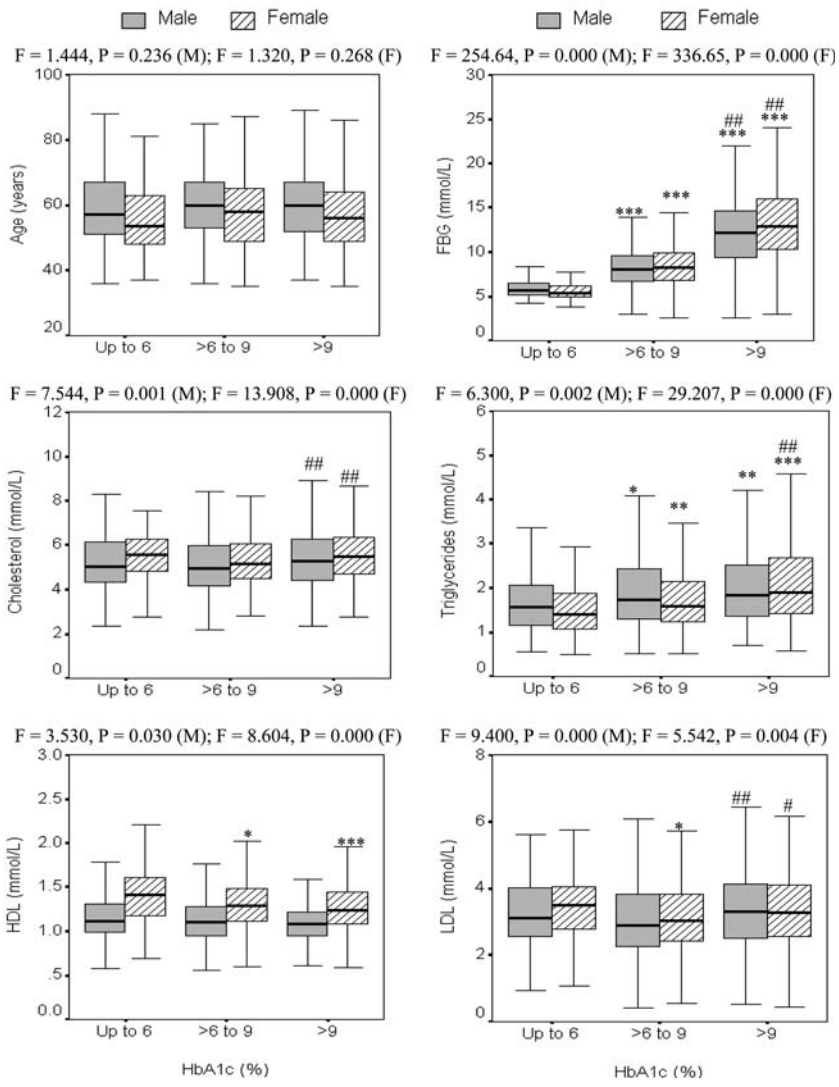

Fig. 2 Patterns of various parameters with respect to glycemic control in male and female type 2 diabetic patients. *Box plots* show the median (*middle horizontal line*), interquartile range (*box*) and minimum and maximum values (*vertical lines*). ANOVA *F* and *P* values for male (M) and female (F) are also shown. $*P < 0.05$, $**P < 0.01$ and $***P < 0.001$ versus $HbA_{1c} \leq 6\%$ group; $\#P < 0.05$ and $\#\#P < 0.001$ versus HbA_{1c} >6–9% group (Dunnett's test)

There was a slight increase (2.53%) in HbA_{1c} in patients aged 51–70 years as compared to patients aged ≤50 years (Table 3). Older patients (>70 years) had HbA_{1c} levels similar to the younger ones. However, there was neither a significant difference in HbA_{1c} among the four age categories (Table 3) nor a significant correlation between age and HbA_{1c} (Fig. 1), which is supported by earlier study [37]. The magnitude of hyperglycemia was significantly less in patients aged >70 years, whereas the average FBG levels in the remaining patients (aged 35–70 years) were more or less same (Table 3). An earlier study also showed no variability in hyperglycemia with age [38]. There was a significant decrease in various lipid components including total cholesterol, triglycerides and LDL with advancing age (Table 3). However, HDL levels remained stable and did not vary appreciably among the patients of different age groups. Our findings are supported by significant increases in total cholesterol, triglycerides and LDL observed in young type 2 diabetic patients with poor glycemic control [39]. Our results, however, are contrary to dyslipidemia in older patients reported earlier; this contradiction may be due to the few numbers of patients (ten in each group) used in that study [38].

Both male and female diabetic patients with uncontrolled diabetes had severe hyperglycemia and significantly increased triglycerides, cholesterol and LDL (Fig. 2). The variation in HDL with respect to glycemic control did not differ significantly among male patients. Whereas, female patients demonstrated proportionate and significant decrements in HDL levels with increasing HbA_{1c} cutoffs (Fig. 2). Earlier study in Saudi type 2 diabetic patients categorized 37 and 28.4% of the total patients as borderline and high-risk group for development of CVD [40]. Recently, Daghash et al. [41] reported significant dyslipidemia in Arabian type 2 diabetic patients as compared to controls. Dyslipidemia may occur in both male and female diabetic patients [42]. Although mild triglyceridemia is a common feature of diabetes, severe triglyceridemia typically occurs in poorly controlled diabetes [43]. High HDL levels protect against CAD development, as patients with high HDL tend to have lower prevalence of CAD risk factors [44]. On the other hand, patients with low levels of HDL are more likely to develop myocardial infraction [45]. High triglycerides and low HDL, but not hypercholesterolemia, are the main features of dyslipidemia observed in patients with metabolic syndrome [46]. Recently, Avogaro et al. [47] have suggested that type 2 diabetic dyslipidemia in females and hyperglycemia in males are important risk factors amenable to more aggressive treatment.

The results of univariate analysis have shown that HbA_{1c} is a good predictor of triglycerides, followed by cholesterol, LDL and HDL (Table 5). It has been reported that HDL cholesterol is inversely, and non-HDL cholesterol directly, associated with CHD risk in diabetes patients [48]. Another study on female type 2 diabetic patients has revealed that association between non-HDL cholesterol and CHD risk is apparent in patients with elevated triglycerides [49]. Moreover, significantly high serum triglyceride levels have been found in diabetic patients with CHD as compared to non-diabetic patients [35]. Onat et al. [50] suggested that fasting triglycerides are predictive for future CVD independent of age, diabetes, total cholesterol and HDL. The above discussion clearly indicates the clinical significance of various lipid parameters including total cholesterol, triglycerides, HDL and LDL in predisposing diabetic patients to cardiovascular complications. Significant correlations between HbA_{1c} and all these lipid parameters (Fig. 1) and a linear relationship between HbA_{1c} and dyslipidemia (Fig. 2) point towards the usefulness of HbA_{1c} for screening high-risk diabetic patients. Furthermore, there were no significant interactions between sex or age and HbA_{1c} with respect to lipid profile (Table 5) suggesting the validity of HbA_{1c} for predicting dyslipidemia irrespective of patient's gender and age.

In conclusion, the findings of this study clearly suggest that HbA_{1c} endures the ability of predicting serum lipid profile in both male and female diabetic patients. Thus, dual biomarker capacity of HbA_{1c} (glycemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients for timely intervention with lipid lowering drugs.

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References

1. Berry C, Tardif JC, Bourassa MG (2007) Coronary heart disease in patients with diabetes: part I: recent advances in prevention and noninvasive management. J Am Coll Cardiol 49:631–642
2. Sultan A, Thuan JF, Avignon A (2006) Primary prevention of cardiovascular events and type 2 diabetes: should we prioritize our interventions? Diabetes Metab 32:559–567
3. Rader DJ (2007) Effect of insulin resistance, dyslipidemia, and intra-abdominal adiposity on the development of cardiovascular disease and diabetes mellitus. Am J Med 120:S12–S18
4. Giansanti R, Rabini RA, Romagnoli F, Fumelli D, Sorichetti P, Boemi M, Fumelli P (1999) Coronary heart disease, type 2 diabetes mellitus and cardiovascular disease risk factors: a study on a middle-aged and elderly population. Arch Genontol Geriatr 29:175–182
5. Jones PH (2006) Clinical significance of recent lipid trials on reducing risk in patients with type 2 diabetes mellitus. Am J Cardiol 99:133–140
6. Smith SC Jr (2007) Multiple risk factors for cardiovascular disease and diabetes mellitus. Am J Med 120:S3–S11

7. Nasri H, Yazdani M (2006) The relationship between serum LDL-cholesterol, HDL-cholesterol and systolic blood pressure in patients with type 2 diabetes. Kardiol Pol 64:1364–1368
8. Gotto AM Jr (2007) Cardiologist's role in improving glucose control and global cardiovascular risk in patients with type 2 diabetes mellitus. Am J Cardiol 99:3–5
9. Miljanovic B, Glynn RJ, Nathan DM, Manson JE, Schaumberg DA (2004) A prospective study of serum lipids and risk of diabetic macular edema in type 1 diabetes. Diabetes 53:2883–2892
10. Davey RA, Tabbutt NC, Favaloro JM, O'Neal DN, Rae D, Zajac JD, Best JD (2006) Severe combined hyperlipidemia and retinal lipid infiltration in a patient with type 2 diabetes mellitus. Lipids Health Dis 5:29–33
11. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE (2002) Defining the relationship between plasma glucose and HbA1c: analysis of glucose profiles and HbA1c in the Diabetes Control and Complications trial. Diabetes Care 25:275–278
12. Selvin E, Coresh J, Golden SH, Brancati FL, Folsom AR, Steffes MW (2005) Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. Arch Intern Med 165:1910–1916
13. Selvin E, Coresh J, Shahar E, Zhang L, Steffes M, Sharrett AR (2005) Glycemia (haemoglobin A1c) and incident of ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Lancet Neurol 4:821–826
14. Ravipati G, Aronow WS, Ahn C, Sujata K, Saulle LN, Weiss MB (2006) Association of hemoglobin A1c level with the severity of coronary artery disease in patients with diabetes mellitus. Am J Cardiol 97:968–969
15. Selvin E, Wattanakit K, Steffens MW, Coresh J, Sharrett AR (2006) HbA1c and peripheral arterial disease in diabetes: the Atherosclerosis Risk in Communities study. Diabetes Care 29:877–882
16. Kawasumi M, Tanaka Y, Uchino H, Shimizu T, Tamura Y, Sato F, Mita T, Watada H, Sakai K, Hirose T, Kawamori R (2006) Strict glycemic control ameliorates the increase of carotid IMT in patients with type 2 diabetes. Endocr J 53:45–50
17. Woodward A, Wallymahmed M, Wilding J, Gill G (2005) Improved glycemic control: an unintended benefit of a nurse-led cardiovascular risk reduction clinic. Diabet Med 22:1272–1274
18. Nakamura K, Yamagishi SI, Adachi H, Kurita-Nakamura Y, Matsui T, Yoshida T, Sato A, Imaizumi T (2007) Elevation of soluble form of receptor for advanced glycation end products (sRAGE) in diabetic subjects with coronary artery disease. Diabetes Metab Res Rev 23(5):368–371
19. Rosediani M, Azidah AK, Mafauzy M (2006) Correlation between fasting plasma glucose, post prandial glucose and glycated haemoglobin and fructosamine. Med J Malaysia 61:67–71
20. Akbar DH, Ahmed MM, Algamdi AA (2003) Cardiovascular risk factor in Saudi Arabian and non-Saudi Arabian diabetic patients in Saudi Arabia. East Medit Health J 9:884–892
21. Ciardullo AV, Azzolini L, Bevini M, Cadioli T, Malavasi P, Morellini A et al (2004) Non-HDL cholesterol predicts coronary heart disease in primary prevention: findings from an Italian 40–69-year-old cohort in general practice. Monaldi Arch Chest Dis 62:69–72
22. Ito C, Maeda R, Ishida S, Sasaki H, Harada H (2000) Correlation among fasting plasma glucose, two-hour plasma glucose levels in OGTT and HbA1c. Diabetes Res Clin Pract 50:225–230
23. Ko GT, Chan JC, Woo J, Lau E, Yeung VT, Chow CC, Li JK, So WY, Chan WB, Cockram CS (1998) Glycated hemoglobin and cardiovascular risk factors in Chinese subjects with normal glucose tolerance. Diabet Med 15:573–578
24. Ladeia AM, Adan L, Couto-Silva AC, Hiltner A, Guimaraes AC (2006) Lipid profile correlates with glycemic control in young patients with type 1 diabetes mellitus. Prev Cardiol 9:82–88
25. Faulkner MS, Chao WH, Kamth SK, Quinn L, Fritschi C, Maggiore JA, Williams RH, Reynolds RD (2006) Total homocysteine, diet and lipid profiles in type 1 and type 2 diabetic and non-diabetic adolescents. J Cardiovasc Nurs 21:47–55
26. Chan WB, Tong PC, Chow CC, So WY, Ng MC, Ma RC, Osaki R, Cockram CS, Chan JC (2005) Triglyceride predicts cardiovascular mortality and its relationship with glycemia and obesity in Chinese type 2 diabetic patients. Diabetes Metab Res Rev 21:183–188
27. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M (1998) Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 339:229–234
28. Gu K, Cowie CC, Harris MI (1999) Diabetes and decline in heart disease mortality in US adults. JAMA 281:1291–1297
29. Walden C, Knopp R, Wahl P, Beach K, Strandness E (1984) Sex differences in the effect of diabetes mellitus on lipoprotein triglyceride and cholesterol concentrations. N Engl J Med 311:953–959
30. Howard B, Cowan L, Go O, Welty T, Robbins D, Lee E (1998) Adverse effects of diabetes on multiple cardiovascular disease risk factors in women: the Strong Heart Study. Diabetes Care 21:1258–1265
31. Steinberg HO, Paradisi G, Cronin J, Crowde K, Hempfling A, Hook G, Baron AD (2000) Type II diabetes abrogates sex differences in endothelial function in pre-menopausal women. Circulation 101:2040–2046
32. Wexler DJ, Grant RW, Meigs JB, Nathan DM, Cagliero E (2005) Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes. Diabetes Care 28:514–520
33. The Diabetes Prevention Program Research Group (2005) Lipid, lipoproteins, C-reactive protein, and hemostatic factors at baseline in the diabetes prevention program. Diabetes Care 28:2472–2479
34. Mohamad M, Arshad F, Noor MIM, Ali R (1997) Prevalence of dyslipidemia in non-insulin-dependent diabetic patients attending armed forces clinics in Kuala Lumpur. Asia Pacific J Clin Nutr 6:203–206
35. Esteghamati A, Abbasi M, Nakhjavani M, Yousefizadeh A, Basa AP, Afshar H (2006) Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. Cardiovasc Diabetol 5:15
36. Sibley SD, Thomas W, de Boer I, Brunzell JD, Steffes MW (2006) Gender and elevated albumin excretion in the Diabetes Control and Complications trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort: role of central obesity. Am J Kidney Dis 47:223–232
37. Doruk H, Mas MR, Ateskan U, Isik AT, Saglam M, Kutlu M (2005) The relationship between age ad carotid artery intima-media thickness, hemoglobin A1c in nondiabetic, healthy geriatric population. Arch Gerontol Geriatr 41:113–119
38. Kalofoutis C, Piperi C, Zisaki A, Singh J, Harris F, Phoenix D, Alaveras A, Kalofoutis A (2006) Differences in expression of cardiovascular risk factors among type 2 diabetes mellitus patients of different age. Ann N Y Acad Sci 1084:166–177
39. Petitti DB, Imperatore G, Palla SL, Daniels SR, Dolan LM, Kershnar AK et al (2007) Serum lipids and glucose control: the SEARCH for Diabetes in Youth study. Arch Pediatr Adolesc Med 161:159–165
40. El-Hazmi MA, Al-Swailem AR, Warsy AS, Al-Meshari AA, Sulaimani R, Al-Swailem AM, Magbool GM (1999) Lipids and related parameters in Saudi type II diabetes mellitus patients. Ann Saudi Med 19:304–307
41. Daghash MH, Bener A, Zirie M, Dabdoub W, Al-Hamaq AO, Al-Arabi ZA (2007) Lipoprotein profile in Arabian type 2 diabetic patients: relationship to coronary artery diseases. Int J Cardiol (in press)

42. Lin SD, Tu ST, Hsu SR, Lin KC, Sheu WH (2006) Characteristics predicting dyslipidemia in drug-naive type 2 diabetes patients. J Chin Med Assoc 69:404–408
43. Smellie WS (2006) Hypertriglyceridaemia in diabetes. BMJ 333:1257–1260
44. DeFaria Yeh D, Freeman MW, Meigs JB, Grant RW (2007) Risk factors for coronary artery disease in patients with elevated high-density lipoprotein cholesterol. Am J Cardiol 99:1–4
45. Sun YH, Yang YJ, Pei WD, Wu YJ, Gao RL (2006) Patients with low high-density lipoprotein-cholesterol or smoking are more likely to develop myocardial infarction among subjects with a visible lesion or stenosis in coronary artery. Circ J 70:1602–1605
46. Bellomo A, Mancinella M, Troisi G, Ettorre E, Marigliano V (2007) Diabetes and metabolic syndrome (MS). Arch Gerontol Geriatr 44:61–67
47. Avogaro A, Giorda C, Maggini M, Mannucci E, Raschetti R, Lombardo F et al (2007) Incidence of coronary heart disease in type 2 diabetic men and women: impact of microvascular complications, treatment and geographic location. Diabetes Care 30(5):1241–1247
48. Eshaghian S, Horwich TB, Fonarow GC (2006) An unexpected inverse relationship between HbA1c levels and mortality in patients with diabetes and advanced systolic heart failure. Am Heart J 151:91
49. Schulze MB, Shai I, Manson JE, Li T, Rifai N, Jiang R, Hu FB (2004) Joint role of non-HDL cholesterol and glycated haemoglobin in predcting future coronary heart disease events among women with type 2 diabetes. Diabetologia 47:2129–2136
50. Onat A, Sari I, Yazici M, Can G, Hergenc G, Avci GS (2006) Plasma triglycerides, an independent predictor of cardiovascular disease in men: a prospective study based on a population with prevalent metabolic syndrome. Int J Cardiol 108:89–95