# Correlation between HbA1c Values and Lipid Profile in Saudi Type 2 Diabetic Patients

## Syed M Farid

### Abstract

**Aim:** This study was designed to evaluate the correlation between levels of HbA1c and various lipid parameters in type2 diabetics of Saudi population. **Method:** Fasting venous blood samples were collected from 110 type2 diabetic patients. The serum was used for analyzing Fasting Blood Glucose (FBG), HbA1c, Total Cholesterol (TC), HDL-cholesterol(HDL-c) and Triglycerides (TG).The risk ratios(TC/HDL-c), LDL-c/HDL-c) were also calculated. The patients were classified into two groups depending on their HbA1c: Good Glycemic Control (GCC) group having HbA1c <7.0% (n=24) and Poor Glycemic Control (PGC) group having HbA1c >7.0% (n=86). **Results:** Patients with HbA1c value>7.0% had significantly higher values of TC, TG, LDL-c, LDL-c/HDL-c ratio and risk ratio (TC/HDL-c) as compared to the patients with HbA1c <7.0%. However, there was no significant difference in values of HDL-c between the two groups. Statistically significant positive correlation was observed between HbA1c and TC, LDL-c, LDL-c/HDL-c ratio, non-HDL-c and risk ratio. The correlation of HbA1c with TG was positive and statistically significant. **Conclusion:** These findings indicate that HbA1c can be utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

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### Introduction

Diabetes is a metabolic disorder resulting either from insulin deficiency or insulin resistance. Diabetic mellitus (DM) is a global epidemic with rapidly increasing prevalence in both developing and developed countries. It is becoming more and more prevalent in Saudi society. In Saudi Arabia, almost one Saudi in four beyond the age of 30 has DM. It is projected that it will be 40-50% in 2020 *(Al-Gannass, 2009)*. Diabetes is more prevalent among Saudis living in urban areas (25.5%) compared to rural Saudis (19.5%) and 90% of diabetics suffer from type 2 diabetes mellitus (T2 DM). Economic drift and its consequent changes in lifestyle in the kingdom have led to this alarming increase in the prevalence of diabetes which has now become the greatest health threat *(Al-Shehriet al.,2013).*The cost of diabetes is challenging health system even in the wealthiest countries. In low-income countries, it threatens to reverse health and economic progress made towards the Millennium Development Goals *(Hashemniaet al., 2012;IDF, 2010)*. Many epidemiological studies have demonstrated that diabetes is well known risk factor for developing cardiovascular and cerebrovascular disease in general population *(Bener & Zirie, 2007)*. The main contributory factors for these complications are uncontrolled DM and dyslipidemia. The dyslipidemia seen in DM patients are characterized by increased triglycerides level, high low density lipoproteins, and low high density lipoproteins. Worsening of glycemic control deteriorates lipid and lipoprotein abnormalities and particularly of DM. The American Diabetes Association(ADA) has designated HbA1c level of<7% as a goal of optimal blood glucose control *(ADA,2003).*Estimated risk of CVD has shown to be increased by18% for each1% increase in absolute HbA1c value in diabetic

population *(Selvin et al., 2006)*. The Diabetes Complications and Control Trial (DCCT) established glycated hemoglobin(HbA1c) as the gold standard of glycemic control, with level $\leq 7\%$ deemed appropriate for reducing the risk of vascular complications *(Gatto,2007)*.HbA1c is directly related to the severity of coronary artery disease (CAD) in diabetic patients *(Ravipati, 2006)*. The abnormalities like insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, and hypertension in type2 diabetics tend to cluster and are often referred to as the "metabolic syndrome". Elements of the metabolic syndrome are strong risk factors for cardiovascular disease. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality *(Singh&Kumar, 2011)*. Thus, the aim of this study was to observe the relationship among glycated hemoglobin (HbA1c) and lipid profile in type 2 diabetics of Saudi population.

**Materials and Methods**

A total of 110 (60male and 50 female) non-obese, non-hypertensive patients of T2DM with no other cardiovascular, renal or thyroid ailments attending King Abdulaziz University health clinic were enrolled in this study. After obtaining informed consent from patients, detailed history was taken followed by thorough physical examination and laboratory investigation. The study protocol was approved by institutional ethical committee. Venous samples were collected from all the patients after at least 10hours fasting into centrifuge tubes. The blood sample was allowed to clot and then centrifuged at 3000 rpm for 15 minutes at room temperature. The sera were analyzed for glycated hemoglobin(HbA1c), fasting serum glucose(FSG), total cholesterol(TC), triglycerides(TG) and high-density lipoprotein cholesterol (HDL- c) using an auto-analyzer (Roche Modular P-800, Germany). Serum low-density lipoprotein cholesterol (LDL-c) was calculated by Frederickson formula. Non- HDL-c, Risk ratio (TC/HDL-c), LDL- c/HDL-c were calculated from the essential lipid profile values. For serum lipid reference level, National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guideline was referred (NCEP, 2013). According to NCEP ATP III guideline, hypercholesterolemia is defined as TC> 200mg/dl, high LDL-c when value>100 mg/dl, hypertriglyceridemia>150mg/dl and low HDL-c when value<40mg/dl.Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration *(Mahato,2011)*. Diabetes was defined as per American Diabetes Association *(ADA)* criteria. Value of HbA1c was given as percentage of total hemoglobin and values of all other parameters were given in mg/dl. Statistical analysis was done by SPSS version17.0. Pearson's correlation test was performed to examine correlations between various parameters. Independent sample test (2-tailed ) was used to compare means of different parameters. All values are expressed as mean± SD. The results were considered significant when $p< 0.05$.

**Results**

**Table 1. Lipid Profile Parameters of Male and FemaleType2 Diabetic Patients**

| Paratermeter | Males N=60 Mean ±Sd | Females N=50 Mean ±Sd | P-Value |
|---|---|---|---|
| Age,yrs | 60.08±6.29 | 58.05±5.88 | 0.206 |
| FBG, mg/dl | 183.06±62.82 | 193.86±66.96 | 0.349 |
| HbA1c,% | 8.75±1.26 | 9.19±1.78 | 0.211 |
| TC, mg/dl | 177.32±23.44 | 187.28±27.25 | 0.043* |
| TG, mg/dl | 164.10±21.82 | 159.35±18.74 | 0.526 |
| HDL-c,mg/dl | 36.47±6.27 | 36.94±5.70 | 0.609 |

2

| LDL-c,mg/dl | 95.14±7.25 | 101.52±7.55 | 0.004* |
|---|---|---|---|

*Statistically significant

**Table 2. Biochemical parameters categorized by patients' glycemic control (HbA1c)**

| Paratermeter | Glycated Hemoglobin(Hba1c) | | P-Value |
|---|---|---|---|
| | ≤ 7% <br> n=24 <br> Mean±SD | >7% <br> n=86 <br> Mean±SD | |
| TC, mg/dl | 176.11±18.92 | 188.18±23.82 | 0.025* |
| TG, mg/dl | 152.15±12.85 | 164.42±21.52 | 0.040* |
| HDL-c,mg/dl | 36.17±6.32 | 36.99±5.97 | 0.482 |
| LDL-c,mg/dl | 95.92±8.45 | 98.30±7.73 | 0.012* |
| Risk ratio,    TC/ HDL-c | 3.93±0.96 | 4.19±1.15 | 0.040* |
| Non HDL-c, mg/dl | 145.39±19.47 | 151.26±25.12 | 0.032* |
| LDL-c/ HDL-c | 2.77±0.62 | 3.57±1.02 | 0.044* |
| FBG, mg/dl | 142.66±43.17 | 197.82±67.02 | 0.000* |

*Statistically significant

One hundred ten type 2 diabetic subjects included in the study out of which 60 were male and 50 were female. The mean age±SD of male and female were 60.08±6.29 and 58.05± 5.88years respectively. The mean value of HbA1c and FBG were higher in females in comparison to male patients but the differences were not significant. Among the circulating lipids, TC and LDL-c were significantly higher($p< 0.05$) in females than male patients. Although the mean level of TG was slightly lower and of HDL-c slightly higher in females than males, these differences were statistically. Hypercholesterolemia was found in 23 (20.9%) individuals, hypertriglyceridemia was found in 68 (61.8%) individuals, decreased HDL-c was found in 67(60.9%) individuals and increased LDL-c was found in 48(43.6%) individuals. Among the diabetic individuals, 31 (28.2%) individuals had only one abnormal lipid profile parameter, 44(40%) had two abnormal lipid parameterand 21 (19.1%) individuals had three abnormal lipid profile parameter. According to NCEP ATPIIIguidelines, 50 (83.3%) males out of 60 and 40 (80%) females out of 50 were dyslipidemic. Table 2 shows classification of diabetic patients into two groups as per their glycemic index. First group consists of patients with HbA1c value≤7.0% and second group consists of patients with HbA1c value>7.0%. Patients with HbA1c>7.0% had significantly higher values of TC, TG, LDL-c, Non-HDL-c, LDL-c/HDL-c ratio and risk ratio as compared to patients with value ≤7.0%.  Statistically significant positive correlation was observed between FBG and HbA1c (p=0.000,r= 0.783). HbA1c also demonstrated direct and significant correlation with total cholesterol (p=0.000,r=0.281), LDL-c (p=0.000,r=0.317), LDL-c/HDL-c ratio (p = 0.000, r=0.21), Non-HDL-c (p = 0.000, r = 0.211) and Risk ratio (p=0.000, r= 0.223).The correlation of HbA1c with TG was positive (p = 0.037, r= 0.016) and statistically significant. HbA1c showed statistically non-significant negative correlation with HDL-c (p= 0.824,r=-0.005).

**Discussion**

In the present study, the usual lipid profile, fasting blood glucose and glycated hemoglobin were investigated. The distribution of subjects according to gender and specific HbA1c cut offs showed that most of the type2 diabetic patients experience poor glycemic control irrespective of their

gender (Table1).The values of HbA1c and FBG did not differ significantly between male and female subjects. A highly significant correlation between HbA1c and FBG observed in this study is similar with previous studies *(Al- Alawi;2014;Reddy,2014;Ahmedetal., 2013)*. We also observed significant correlation between HbA1c and total cholesterol, TG, and LDL-c.In various studies HbA1c was found to have positive correlation with TC,TG and LDL-c in diabetic patients *(Al-Alawi;2014;Reddy, 2014;Ahmed,2013; Pujari,2013; Rosediani,2006).*In the present study, the association between HbA1c and various lipid parameters and LDL-c/HDL-c ratio suggests the importance of glycemic control in order to control dyslipidemia. Although the levels of HbA1c and FBS did not differ significantly between the two genders, female patients showed higher levels of both (Table1).Diabetes confers a markedly increased risk of cardiovascular events in both males and females *(Haffner etal.,1998).*However, women with diabetes are more susceptible to increased cardiovascular mortality (Guetal.,1999). Diabetic women may be subject to more adverse changes in coagulation, vascular function and cardiovascular risk factors than diabetic men(Steinberg etal.,2000). The results of this study for lipid profile showed that female diabetic patients had significantly higher levels of cholesterol and LDL-c. This is in agreement with the previous reports*(Wexleretal.,2005; Esteghamatietal.,2006).* Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, leading to differences in altered lipoproteins*(Sibley etal., 2006).* The present study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-c and low HDL-c levels and these are well known risk factors for cardiovascular diseases. Insulin affects the liver apolipoprotein production which regulates the enzymatic activity of lipoproteinlipase (LpL) and cholesterol ester transport protein. All these factors are likely causes of dyslipidemia in diabetes mellitus *(Goldberg, 1996).* Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps to produce altered LpLin DM *(Koetal., 1998).* The present study also showed a statistically significant correlation between HbA1c and non-HDL-c. Non-HDL-c was shown to be the stronger predictor of CVD in type2 diabetes*(Lu etal.,2003).* National Cholesterol Education Program Adult Treatment Panel III has recommended the use of Non-HDL in assessing CVD risk in patients with diabetes.The measurement of Non-HDL-c is simple and can be conducted even in non-fasting state of patients and can be determined regardless of TG concentration. Hence, Non-HDL cholesterol can be of great value in determining dyslipidemia in diabetic subjects. In present study, a significant correlation was noted between risk ratio and HbA1c which is similar to the findings of other studies*(Al-Alawi, 2014;Gimeno- Ornaetal., 2005).*Previous studies revealed that the predictive power of the TC/HDL-c ratio was found to be higher than that of Non-HDL cholesterol and that TC/HDL-c ratio can be used as a guide for the treatment of diabetic dyslipidemia *(Al-Alawi,2014;Gimeno-Orna,2005).* In this context it is worth to state that total number of apo-B containing particles and small LDL-c particles are increased in diabetes and these metabolic abnormalities are better reflected by TC/HDL-c ratio and Non-HDL-c than LDL-c alone*(Lemieuxet al., 2001;Peters,2008).*In the present study, all diabetic patients were categorized into two groups as per the HbA1c cut off of 7.0%. The diabetic patients with HbA1c value>7.0% showed a significant increase in the mean values of TC, LDL-c, TG, LDL-c/HDL-c ratio, Non-HDL-c and Risk ratio without any significant alteration in HDL-c in comparison to patients with HbA1c value≤7.0%.Different authors *(Samathaetal.,2008;Khanetal., 2007;Meenuetal.,2013; Josephine&Kirubakaran,2014)* reported the impact of glycemic control on various lipid parameters in which severity of dyslipidemia increases in patients with higher HbA1c value. *ZheYan etal(2012)* in their study found that TC/HDL-c, LDL-c/HDL-c ratios were gradually increased with increased HbA1c level and the difference was significant among groupsp<0.05).The results of a very recent article *(Abhimanyu&Kondru,2015)* showed that there was a significant increase in Non-HDL

cholesterol (p< 0.001) and LDL-c/HDL-c ratio(p<0.05) in diabetic patients compared to age and sex matched controls. More emphasis should be placed on considering Non-HDL cholesterol and LDL/HDL ratio as markers of diabetic dyslipidemia and cardiovascular risk markers than LDL alone. These parameters are cost effective and affordable comparative to some new markers in assessing cardiovascular risk in diabetic patients. As elevated HbA1c and dyslipidemia are independent risk factors of cardiovascular diseases, diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics*(Selvinet al.,2006;Mahatoetal.,2011;Al-Alawi,2014; Samathaetal.,2008).*It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by10%*(Khaw etal.,2002). Selvinetal. (2006)* revealed that each 1% increase in absolute HbA1c value in diabetic patients increased the risk of CVD by18%. Epidemiological and interventional studies suggest that weight loss is the main driving force to reduce diabetes risk. Landmark clinical trials of lifestyle changes in subjects with diabetes have shown that diet and exercise leading to weight loss consistently reduce the incidence of diabetes*(Walkeretal.,2010; Eckeletal.,2011).* Some studies revealed that continuous energy restriction associated with weight loss significantly improved the lipid profile of high risk patients *(Ditschuneitetal., 2002;Harder etal.,2004).*Improvement in dyslipidemia is sustained with long-term weigh tloss *(Dixon&O'Brine,2012).*Intentional weight loss of 10% of body weight can potentially decrease HBA1c by 0.81% among patients with type2 DM *(Shanthaetal.,2012).* Healthcare providers should invest more effort in encouraging and counseling a patient attempting weight loss.

## Conclusion

Significant correlation between HbA1c and various circulating lipid parameters and significant differences of lipid parameters in two groups (≤7.0%and>7.0%) of glycatedhemoglobin indicates that HbA1c can be used as a potential biomarker for predicting dyslipidemia in type2 diabetic patients in addition to glycemic control and hence early diagnosis can be accomplished through relatively inexpensive blood testing for timely intervention with lipid lowering drugs. Lifestyle modifications and earlier intervention by lipid lowering therapy can reduce the cardiovascular mortality of this risk group. However for intervention by lipid lowering therapy, more prospective studies with large sample sizes are essential.

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