



# Differences In Glycosylated Hemoglobin To Conventional Cardiovascular Risk Factors In Obesity

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## ABSTRACT

**Background:** Glycosylated hemoglobin (HbA1c) has been used as an index for clinical diagnosis of diabetes which is closely related to the complications of cardiovascular. The purpose of the study was to assess the differences in HbA1c against conventional cardiovascular risk in obese patients.

**Method:** This cross-sectional study was conducted on obese patients (BMI > 25). This study included 40 obese patients, whereas those with a history of CVD, thyroid disorders, or currently on lipid-lowering agents were excluded. HbA1c is divided over HbA1c < 5.6 and HbA1c > 5.6 (prediabetes), body mass index (BMI) were measured using standard methods. Laboratory assessment included venous blood samples in a fasted state for the determination of components of the lipid profile [total cholesterol (TC), HDL-C, and TG], HbA1c, homeostatic model assessment for insulin resistant (HOMA-IR) using the formula: insulin x fasting glucose / 405, C-reactive protein (CRP), and adiponectin.

**Result:** 40 obese patients participated in the study with an age of 41.7±6.0 years and a BMI of 33.1±5.0 kg/m<sup>2</sup>, and a significant correlation between HbA1c and age and HOMA-IR. All cardiovascular risk factors tend to increase but increased significantly at age, and TG (p<0.5).

**Conclusion:** In this study, the average HbA1c was significantly correlated with age and HOMA-IR, and all lipid parameters of HbA1c > 5.6 (prediabetes) tended to be higher than normal obesity.

**Keywords:** HbA1c, Obesity, Cardiovascular Risk

## ABSTRAK

**Latar Belakang:** Hemoglobin glikosilasi (HbA1c) telah digunakan sebagai indeks untuk diagnosis klinis diabetes yang terkait erat dengan komplikasi kardiovaskular. Tujuan dari penelitian ini adalah untuk menilai perbedaan HbA1c terhadap risiko kardiovaskular konvensional pada pasien obesitas.

**Metode:** Studi potong lintang ini dilakukan pada pasien obesitas (BMI > 25). Studi ini melibatkan 40 pasien obes, dikecualikan pada mereka yang memiliki riwayat PKV, gangguan tiroid, atau menggunakan obat penurun lipid. HbA1c dibagi atas HbA1c < 5,6 dan HbA1c > 5,6 (prediabetes), indeks massa tubuh (IMT) diukur menggunakan metode standar. Penilaian

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*laboratorium termasuk sampel darah vena dalam keadaan puasa untuk penentuan komponen profil lipid [kolesterol total (TC), HDL-C, dan TG], HbA1c, penilaian model homeostatik untuk insulin resisten (HOMA-IR) menggunakan rumus: insulin x glukosa puasa / 405, protein C-reaktif (CRP), dan adiponektin.*

**Hasil.** Ada 40 pasien obesitas yang berpartisipasi dalam penelitian dengan usia  $41,7 \pm 6,0$  tahun dan IMT  $33,1 \pm 5,0$  kg/m<sup>2</sup>, dan korelasi yang signifikan antara HbA1c dengan usia dan HOMA-IR. Semua faktor risiko kardiovaskular cenderung meningkat, sedangkan yang meningkat secara signifikan adalah usia, dan TG ( $p < 0,5$ ).

**Kesimpulan:** Dalam penelitian ini, rata-rata HbA1c secara signifikan berkorelasi dengan usia dan HOMA-IR, dan semua parameter lipid HbA1c  $> 5,6$  (prediabetes) cenderung lebih tinggi daripada obesitas normal.

**Kata Kunci:** HbA1c, Obesitas, Risiko Kardiovaskular

## 1 Introduction

Diabetes is affecting relatively wide portions of the world population, especially in developed countries, and the complications of diabetes are rising in younger people and earlier [1]. Obesity is an important risk factor for type 2 diabetes. With the improvement of living standards, the number of obese people increases gradually, causing the gradually mounting number of patients with diabetes, as well as the number of younger patients in particular [2]. There are nearly 180 million patients with diabetes in the world [3]. Glycosylated hemoglobin (HbA1c) plays an important role in the management of diabetes, which has been regarded as one of the most important research progress in the treatment of diabetes for decades.[4] HbA1c has been used as an index for the clinical diagnosis of diabetes in foreign countries. However, it is found that the threshold value of HbA1c is not suitable for young people, especially Chinese people.[5] As we know, HbA1c reflects the average blood glucose of about three months, which is closely related to the complications of diabetes.[6] HbA1c is widely used in blood glucose management of gestational diabetes mellitus in addition to the clinical significance of HbA1c for type 1 and type 2 diabetes mellitus.[7] HbA1c is affected by many other factors. The study shows that HbA1c is related to people's lifestyles, such as strenuous exercise and carbohydrate control [8]. It is well proved that HbA1c correlates with the life cycle of red blood cells. Recent studies suggest that the results of HbA1c are affected by iron deficiency anemia and are related to the degree of anemia.[9] However, another study finds that iron supplementation during pregnancy does not affect the level of HbA1c and has no clinical effect on the final interpretation of the results in patients with no anemia or mild anemia.[10] High HbA1c and fasting blood glucose levels are believed to significantly alter the relationship between HbA1c, glucose, and age.[11] On the other hand, HbA1c is also considered to be a risk factor for cardiovascular disease in patients.[12] At present, the research on HbA1c mostly focuses on the control of diabetes and the standard of detection. Many studies believe that HbA1c is related to many factors, but the results are controversial. Therefore, we designed this study, hoping to clarify the correlation between HbA1c and other factors through the analysis of big data, such as gender, age, fatty liver, and biochemical

indicators, and to further investigate the risk factors affecting HbA1c, in a bid to lay a foundation for the study of HbA1c-related diseases and chronic disease management.

Circulating hemoglobin A1c (HbA1c) indicates average blood glucose concentrations over the preceding 3 months. The absence of the need for patients to fast for HbA1c assessment is a major advantage of measuring HbA1c for screening for dysglycemia, including diabetes and prediabetes, and has been endorsed for such screening by society recommendations.[13] Whether screening HbA1c values incrementally contributes to cardiovascular disease (CVD) risk assessment and prognostication beyond established risk predictors in patients without diabetes remains uncertain, with a meta-analysis of observational data suggesting the independent prognostic utility of HbA1c.[14] The European Systematic COronary Risk Evaluation (SCORE) CVD risks score,[15] QRISK3 risk score,[16] and the American College of Cardiology/American Heart Association (ACC/AHA) CVD risk score [17] currently do not include any specific measure of glycemia in their risk prediction models and include only diabetes as a categorical entity. In support of this approach, an individual participant meta-analysis of nearly 300,000 participants without diabetes or known CVD at baseline suggested that HbA1c added a very modest discriminative ability to CVD risk estimation methods that use conventional risk factors.[18] However, such work has been based on either relatively small single cohorts or multiple cohorts with considerable interstudy heterogeneity. The lack of data from a single large cohort with consistent phenotyping of exposures and events is a limitation in interpreting the existing literature on this topic. This topic requires better evidence to inform clinical care. Capitalizing on the availability of data in the UK Biobank comprising several hundred thousand participants including baseline HbA1c measures and capture of longitudinal clinical outcomes, we examined the prognostic utility of HbA1c for CVD in participants without prevalent diabetes.

## 2 Method

This cross-sectional study was conducted on obesity (BMI > 25). Informed written consent was obtained after explaining the nature of the study to the patients, and ethical clearance was obtained.

This study included 40 obese patients, whereas those with a history of CVD, thyroid disorders, or currently on lipid-lowering agents were excluded. HbA1c is divided over HbA1c < 5.6 and HbA1c >5.6 (prediabetes), and body mass index (BMI) was measured using standard methods. Laboratory assessment included venous blood samples in a fasted state for the determination of components of the lipid profile [total cholesterol (TC), HDLC, and TG], HbA1c, homeostatic model assessment insulin resistant (HOMA-IR) using the formula of fasting insulin x fasting glucose/405, C-reactive protein (CRP), and adiponectin.

## Statistical analysis

Statistical analysis was done using the SPSS package and MS excel. Pearson correlation or Spearman correlation test and p values were calculated. P values <0.05 was considered.

### 3 Result

Based on table 1, 40 obese patients participated in the study with an age of  $41.76.0 \pm$  years and a BMI of  $33.15.0 \pm$  kg/m<sup>2</sup>.

**Table 1** Baseline data on Obese Patients

Parameter	n=40
Age (yr)	41.7±6.0
BMI (kg/m <sup>2</sup> )	33.1± 5.0
HbA1c (%)	5.6±0.8
HOMA-IR	1.1±0.9
LDLC (mg/dl)	136.7± 34.7
HDLC (mg/dl)	47.6±12.9
TG (mg/dl)	150.2±58.4
CRP (mg/L)	3.8±2.4
Adiponectin (ug/mL)	4.0±2.1

Abbreviations: BMI: body mass index; HbA1c: hemoglobin A1c; LDLC: low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TG: triglyceride; CRP: C-reactive protein.

In table 2, there is a significant correlation between HbA1c and age and HOMA-IR

**Table 2** The correlation between HbA1c and cardiovascular risk factors

Parameter	r	p
Age (yr)	0.429	0.006*
BMI (kg/m <sup>2</sup> )	0.053	0.747
HOMA-IR	0.375	0.017*
LDLC (mg/dl)	0.217	0.180
HDLC (mg/dl)	-0.214	0.185
TG (mg/dl)	0.194	0.229
CRP (mg/L)	0.179	0.269
Adiponectin (ug/mL)	0.078	0.632

Abbreviations: BMI: body mass index; HbA1c: hemoglobin A1c; LDLC: low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TG: triglyceride; CRP: C-reactive protein.

In table 3, all cardiovascular risk factors tend to increase, but increased significantly at age, TG (p<0.5), and decreased significantly in HDL

**Table 3** Differences in cardiovascular risk factors between Obesity and Prediabetes

Parameter	HbA1c $\leq 5.6$ (n=24)	HbA1c $> 5.6$ (n=16)	P
Age (yr)	39.7 $\pm$ 6.03	44.8 $\pm$ 4.6	0.006*
BMI (kg/m <sup>2</sup> )	32.6 $\pm$ 5.5	33.8 $\pm$ 4.2	0.480
HOMA-IR	0.9 $\pm$ 0.6	1.2 $\pm$ 0.9	0.319
LDLC (mg/dl)	130.2 $\pm$ 30.9	146.7 $\pm$ 38.6	0.142
HDLc (mg/dl)	51.1 $\pm$ 15.3	42.3 $\pm$ 5.0	0.033*
TG (mg/dl)	131.5 $\pm$ 52.7	178.1 $\pm$ 56.7	0.011*
CRP (mg/L)	3.4 $\pm$ 2.4	4.4 $\pm$ 2.4	0.186
Adiponectin (ug/mL)	3.8 $\pm$ 2.4	4.3 $\pm$ 1.7	0.590

Abbreviations: BMI: body mass index; HbA1c: hemoglobin A1c; LDLC: low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TG: triglyceride; CRP: C-

#### 4 Discussion

HbA1c level is recommended by the American Diabetes Association (ADA) to be used as an index for the diagnosis of diabetes [19], and it can reflect a blood glucose level of 2-3 months. It is suggested that HbA1c can be used in the diagnosis of diabetes.[20] HbA1c is becoming more and more popular among primary care providers because it has many practical advantages, including convenient sampling, suitable as an indicator of chronic abnormal blood glucose, low individual variation, and favorable laboratory standardization.[21] In 2010, ADA proposed that an HbA1c value of 5.7% - 6.4% can be diagnosed as prediabetes and HbA1c  $\geq 6.5\%$  can be diagnosed as diabetes,[22] which is a criterion for diagnosis recommended by ADA. In our physically examined population, patients with diabetes included drug users and nondrug users, and HbA1c, as an important indicator of blood glucose management, can show that patients with diabetes in the physically examined population do not control blood glucose well. Many previous studies mentioned that there is an important relationship between HbA1c and obesity and lipid disturbances, especially in diabetes patients where they found that HbA1c showed a positive association with glucose and the TG/HDL ratio,[23] these events were more frequent in patients with obesity. Another study also showed a positive relationship between insulin resistance and serum HbA1c levels in obese children.[24] They studied the level of Glycated hemoglobin (HbA1c) in obese diabetics patients and nonobese diabetics patients and the results were different from the above studies. Patients with nonobese diabetics have a higher level of

HbA1c than obese diabetics patients, the frequency of HbA1c in nonobese diabetics patients was  $8.9 \pm 2.9\%$  while in obese diabetics patients is  $8.2 \pm 2.5\%$ , p-value  $< 0.005$ . [25]

In this studies, mean HbA1c significantly correlate with age and HOMA-IR, all parameter lipid of prediabetes tend higher than obesity. Hasil penelitian ini berbeda dengan penelitian lain karena perbedadaan jumlah dan jenis pasien.

## 5 Conclusion.

In this study, the average HbA1c was significantly correlated with age and HOMA-IR, all lipid parameters of HbA1c  $> 5.6$  (prediabetes) tended to be higher than in obesity. The results of this study are different from other studies because of the difference in the number and type of patient studies.

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