Internal Medicine

Association between glycated hemoglobin A1C and nonrenal complications in patients with diabetes mellitus: A single-center observational study.

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Abstract

Introduction: Diabetes is one of the most emblematic public health problems worldwide; a high level of HbA1c represents a significant risk factor for the development of cardiovascular and renal disease, among other conditions. Objectives. To establish nonrenal complications in diabetic patients admitted to a public reference hospital in Guayaquil, Ecuador.

Methods: This descriptive, prospective, correlational, and cross-sectional study included 103 individuals admitted to Teodoro Maldonado Carbo Hospital who met the inclusion criteria between March and September 2022.

Results: The main acute complication was infection (32%), followed by EHH (27.5%). Coronary artery disease, followed by peripheral vascular disease, is among the most common chronic complications. Most patients concomitantly presented with two or more complications more frequently than with only one complication (36% men, 27% women). Upon hospital admission, 75.6% of the patients had HbAc1 values above 7.6%; a 1% increase in HbA1c was associated with a 30% increase in all-cause mortality and a 40% increase in ischemic heart disease.

Conclusions: There was a positive correlation between HbAc1 and nonrenal complications in diabetic patients, with a Pearson coefficient of 0.91% for acute and chronic complications.

Keywords:

MeCS: Diabetes mellitus, glycosylated hemoglobin, nonrenal complications.

Abbreviations

AC-ACORD: Action to Control Cardiovascular Risk in Diabetes (AC-CORD)
DCCT: Diabetes Control and Complications Trial.
CVD: Cerebral vascular event.

Supplementary information

No supplementary materials are declared.

Availability of data and materials

The data sets used and analyzed during the present study are available from the corresponding author upon reasonable request.

Introduction

Type 2 diabetes is the most common type of diabetes in adults (>90%). It is caused by hyperglycemia, usually due to the loss of progressive insulin secretion by some beta cells due to a history of insulin resistance [1, 2]. Most patients are asymptomatic at the time of diagnosis. The prevalence of asymptomatic diagnoses has increased due to improvements in screening and routine laboratory evaluation [3].

Hemoglobin glycosylated (A1C) has been established as a predictive element of cardiovascular risk in epidemiological research (observational studies or analysis secondary trials). The evidence solidifies that the relationship between blood glucose levels and cardiovascular risk extends to the nondiabetic range. According to a meta-analysis of 97 cohort studies with a median follow-up of 9.8 years, prediabetes (IFG, IGT or increases in A1C in the nondiabetic range [5.7 to 6.4% or 6.0 to 6.4%]) combined with normoglycemia was associated with an increased risk of mortality (risk difference absolute 7.36 per 10,000 person-years, risk relative, 95% 1.10-1.17, coronary heart disease (6.59 per 10,000 person-years) and stroke (3.68 per 10,000 person-years) [4].

Although there is a correlation between hyperglycemia and cardiovascular risk, its addition to conventional cardiovascular risk factors is not associated with clinically significant improvements in risk prediction in type 2 diabetes patients. An analysis of patient data from 73 prospective studies (294,998 participants) showed that adding A1C to forecasting models containing conventional cardiovascular risk factors (age, sex, blood pressure, total and high lipoprotein cholesterol density, smoking) significantly improved the capacity of models to predict cardiac disease development; however, the incremental improvement was slight and scarcely relevant. The improvement provided by A1C was at least equal to improvements estimated for measuring the glucose levels at fasting, random, or postload. These findings suggest that in individuals without known cardiovascular disease or diabetes, traditional cardiovascular risk factors are predictors of more muscular cardiovascular disease than blood glucose measurements. The coincidence and relationship between hyperglycemia and daily risk factors and their contributions can be particularly challenging. Furthermore, there is little evidence that mild hyperglycemia treatment in the prediabetic range reduces the risk of CVD. In individuals with type 1 diabetes, the extent of blood glucose in the A1C plays a substantial role in the risk of cardiovascular disease, as blood glucose only increases with age in the hierarchy of risk factors [5].

The option of a suitable hemoglobin glycosylated (A1C) must be individualized, balancing the reduction in microvascular and macrovascular complications with the time risks of immediate symptoms of hypoglycemia and weight gain. An objectively reasonable therapy could be an A1C value of ≤7% for most patients (using a trial aligned with the Diabetes Control and Complications Trial (DCCT)) whose upper limit of normal is 6%). A glucose level of 70-120 mg/dL (3.9-6.7 mmol/L) and a postprandial glucose level (90-120 minutes after a meal) of less than 180 mg/dL (10 mmol/L) were reached. The A1C goal was the study's objective, but the higher levels achieved may be suitable. If possible, further accurate goals, such as <6.5%, are reasonable to achieve safe results, but no trial data showing that clinicians who support the best long-term clinical results are strict.

For hemoglobin, the treatment goal of hemoglobin A1C should be slightly more significant (e.g., <7.5 or <8%) for patients with a history of severe hypoglycemia or hypoglycemic coma, patients with a limited life expectancy, children with minor or adult elderly individuals, and people with advanced illness.

On the other hand, this indicated an increase in the intensity of glycemic control required to achieve A1C levels substantially below the 7% threshold during pregnancy in women with type 1 diabetes (and in women with type 2 diabetes and shape atypical diabetes) since the A1C level in nondiabetic women decreases physiologically during pregnancy, and the benefits demonstrated to the fetus and neonate drive these goals.

It is known that the risk of retinopathy in diabetic patients does not stop at an A1C value of 7%. The DCCT study established a risk gradient between levels of chronic hemoglobin glycosylated A1C and retinopathy, so for every 1% less HbA1C (for example, from 10 to 9% or from 9 to 8.1%), the risk of retinopathy progression decreases by 15%. The relationship extends throughout the A1C range, so reducing A1C from 7 to 6.3% further reduces the risk of retinopathy between 25% and 35%. However, with additional low A1C results, the benefits of absolutes are reduced progressively at the cost of an increased risk of hypoglycemia [6].

The general objective of this research was to establish non-renal complications in diabetic patients admitted to the Teodoro Maldonado Carbo Hospital in Guayaquil, Ecuador, and characterize the hemoglobin range of glycosylated A1C plus frequency upon admission in patients with decompensated diabetes.

Materials and methods

Study design

The present study is observational and cross-sectional. The source is retrospective.

Scenery

The study was conducted in the Endocrinology Service of the Teodoro Maldonado Specialty Hospital of the Ecuadorian Institute of Social Security in Guayaquil, Ecuador, from March 1, 2022, to September 30, 2022.

Participants

Adult patients with a diagnosis of type 1 or 2 diabetes mellitus admitted with complications of their disease were included. Patients with renal complications were excluded, and patients with incomplete data were excluded from the analysis.

Variables

The variables included age, sex, personal history, HbA1C level, the presence of acute complications (diabetic ketoacidosis, nonketotic hyperosmolar hyperglycemic coma, lactic acidosis, and infections), and the presence of chronic complications (retinopathies, neuropathies, coronary artery disease, peripheral vascular disease, and cerebral vascular disease).

Data sources/measurements

The source was indirect; an electronic form was completed using data from the institutional medical history (AS400) of the patients who entered the hospitalization period. The information was treated confidentially. No personal data were included to identify the study subjects.

Biases

To avoid interviewer, information, and memory biases, the principal investigator always maintained the data with a guide and records approved in the research protocol. Observation and selection bias were avoided by applying participant selection criteria. Two researchers independently analyzed each record in duplicate, and the variables were registered in the database once their agreement was verified.

Study size

The sample was nonprobabilistic, and all patients from the study period were included.

Quantitative variables

Descriptive statistics were used. The results are expressed as frequencies and percentages.

Statistical analysis

Noninferential and inferential statistics were used. For descriptive analysis, frequencies and percentages are presented. Statistical comparisons between proportions were performed with chi-square tests. The association coefficients between the variables were calculated with Pearson's R. The statistical package was IBM Corp. Released in 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

Results

Participants

A total of 103 cases were analyzed.

Main characteristics of the study group

Of the 103 patients, 12 (12%) had type I diabetes mellitus, and 91 (88%) had type 2 diabetes mellitus; in most cases, 70 were men and women. There were 33 patients (Table 1). The average age was 60 ± 6 years. The most frequent comorbidities were arterial hypertension in 38 patients (36.9%), dyslipidemia in 7 patients (6.8%), obesity in 3 patients (2.9%) and smoking in 3 patients (2.9%). Hemoglobin A1c at admission was equal to or less than 6.5% in 7.8% of the patients, from 6.6 to 7.5% in 16.6% of the patients, from 7.6 to 8.5% in 37.8% of the patients, and greater than 9.5% in 37.8% of the patients.

Acute complications

Hyperglycemic coma was the most prevalent, followed by infections. Complications were more prevalent in patients with hemoglobin levels of glycosylated A1C greater than 9.5% (Figure 1).

Chronic complications

Coronary artery disease was the most prevalent, followed by peripheral vascular disease. Complications were more prevalent globally in men (Figure 2). The complications are presented in Table 1 and Figure 3. The hemoglobin level of glycosylated A1C classifies chronic patients.

The Pearson correlation coefficient between the development of ketoacidosis and the hemoglobin level of glycosylated A1C was 0.91 (P <0.001). For the association with the presence of the state, hyperglycemic hyperosmolar was r=0.90 (P <0.001), acidosis lactic acid was r=0.99 (P <0.001), and infections were r= -0.05 (P =0.72). Pearson's coefficient of association for the presence of 2 or more chronic complications was 0.91 (P <0.001).

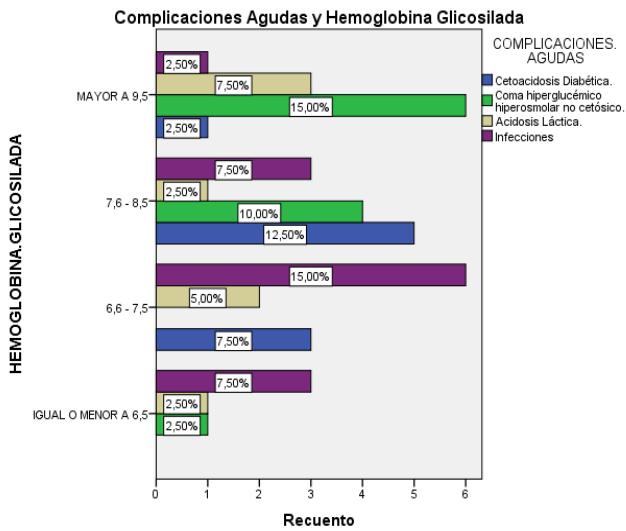**Figure 1 .** Acute complications and glycosylated hemoglobin levels.

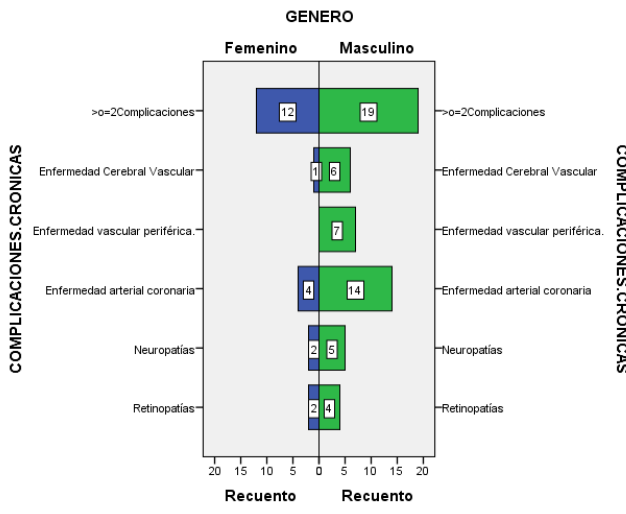**Figure 2.** Chronic complications in the study group were classified by sex.

Table 1. Chronic nonrenal complications and glycosylated hemoglobin values on admission.

	HbA1C <6.6% N=2	HbA1C 6.6-7.5 N=10	HbA1C 7.6-8.5 n=31	HbA1C >9.5 N=33
Retinopathy	1	2	3	0
Neuropathy	0	0	4	3
CAD	1	3	10	4
PVD	0	1	0	6
VBD	0	0	1	6
>=2 C	0	4	13	14

CAD: Coronary artery disease. PVD: Peripheral vascular disease. VBD: Vascular brain disease. C: complications.

Relationship between mortality and glycosylated hemoglobin levels

The highest mortality rate occurred in the hemoglobin group with a glycosylated A1C >9.5% (Figure 4), double that of patients with a glycosylated A1C less than 7.6%. The association coefficient between these variables was 0.42 (P =0.01).

Figure 3 . Representation of glycosylated hemoglobin values and nonrenal chronic complications.
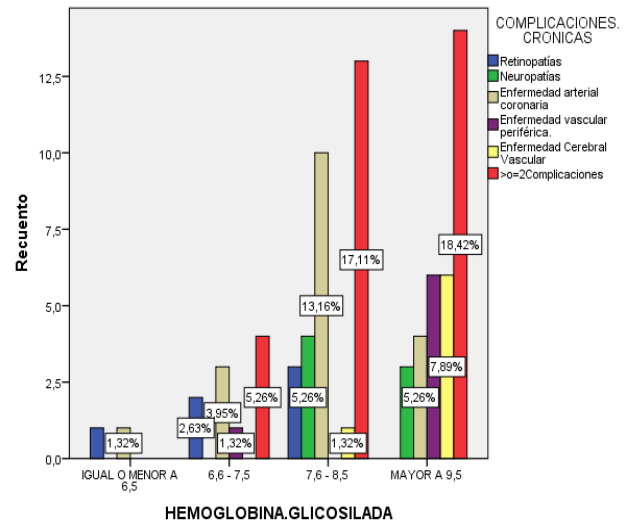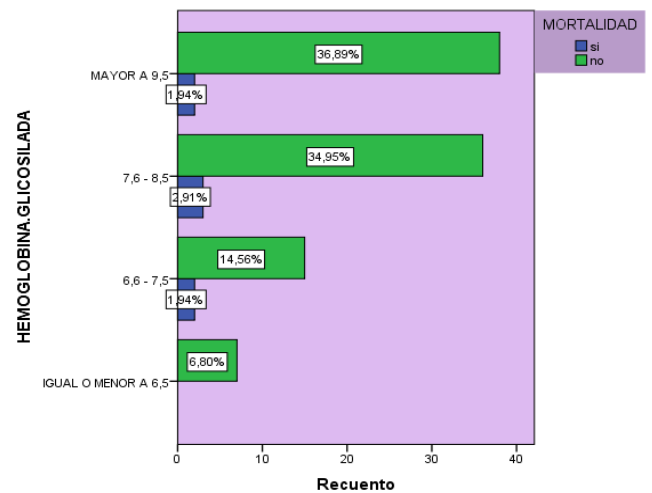

Figure 4. Percent mortality and glycosylated hemoglobin values.

Discussion

The present study describes the relationship between hemoglobin glycosylated A1C and nonrenal complications. The results of a study titled "Action to Control Cardiovascular Risk

in Diabetes (ACCORD)" suggest that a target of hemoglobin glycosylated A1C ranging from 7.0 to 7.9% can be safer for patients with long-standing type 2 diabetes and those who are at high risk for cardiovascular disease (CVD) than a target A1C of less than 6.0% (reaching a median of 6.4%) [7].

A total of 7.0 to 7.9% of patients were affected, supported by the results of a retrospective cohort study of 27,965 patients with type 2 diabetes aged 50 years or older whose treatment had intensified. After a mean follow-up of approximately 4.5 years, mortality by all causes was bimodal in the two scenarios when the values were less than 6.7% or greater than 9.9%, while a value close to 7.5% was associated with mortality by all causes further lower. There was a U-shaped relationship between A1C and mortality, with an increased mortality risk related to A1C values less than 6.5% or greater than 8% [8].

All guidelines recommend fitting the A1C goals for patients individually. The consensus algorithm of the American Diabetes Association (ADA) and the Association European for Diabetes Study (EASD) recommends an A1C of less than 7% for most nonpregnant adults due to the benefits of reducing microvascular complications. The American College of Physicians recommends an A1C between 7% and 8%. The American Geriatrics Society suggested an A1C goal of 8% for adults who are more incredibly frail and people with a life expectancy of less than five years. The recommendations are supported by a decision analysis that integrates multiple prediction models.

At the time of the investigation, 7.6-8.5% of the patients were glycosylated, and greater than 9% presented the most significant number of complications. In this analysis, comorbid conditions and functional deterioration, such as a minor benefit of intensive glucose control over age alone, were the top predictors of life expectancy [9].

In conclusion, we must maintain the optimal hemoglobin level at least one percentage point to control or manage future long-term complications. In our institution, we compare this variable with mortality, revealing a proportional relationship between them.

Various studies have demonstrated that hemoglobin levels greater than 6.5% in patients with diabetes are associated with metabolic anomalies. Hemoglobin is glycosylated in patients with type 1 and type 2 diabetes; in these studies, HbA1c values higher than the reference range were associated with changes such as cognitive deterioration, overweight, metabolic decompensation, and microvascular complications, consistent with the present study.

Conclusions

There was a positive correlation between HbAc1 and morbidity and mortality, with a Pearson coefficient of r=0.91 for acute and chronic complications. The main acute complications were infections (32%) and hyperosmolar hyperglycemic disease (27.5%). Chronic heart disease followed by vasculopathy peripheral to the heart was the main complication. The majority of patients with both acute complications and chronic lesions presented two or more concomitant complications, more frequently than one isolated single complication, with a distribution of 36% in men and 27% in women.

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Statements

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