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ORIGINAL ARTICLE

Relationship between glycated hemoglobin and glucose concentrations in the adult Galician population: selection of optimal glycated hemoglobin cut-off points as a diagnostic tool of diabetes mellitus

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KEYWORDS
HbA_{1c};
Glucose;
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Abstract
Aims/hypothesis: To analyze the relationship between glucose and glycated hemoglobin (HbA_{1c}) in the adult Galician population, evaluate the use of HbA_{1c} for the screening and diagnosis of diabetes, and calculate the diagnostic threshold required for this purpose.
Methods: We analyzed data on 2848 subjects (aged 18–85 years) drawn from a study undertaken in 2004 to assess the prevalence of diabetes in Galicia. For study purposes, diabetes was defined using the criteria recommended in 2002. Participants were classified into four glucose-based groups. The relationship between glucose and HbA_{1c} was described using linear regression models, generalized additive models and Spearman's correlation. Diagnostic capacity was assessed, and optimal HbA_{1c} cut-off points were calculated as a diabetes marker using the receiver operating characteristic curve.

Abbreviations: AUC, area under the curve; FPG, fasting glucose; 2hOGTT, glycemia at 2 h of oral glucose tolerance test; HbA1c, glycated hemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; KDM, known diabetes; NPV, negative predictive value; NGM, normal glucose metabolism; PPV, positive predictive value; ROC, receiver operating characteristic curve; Se, sensitivity; Sp, specificity; UKDM, unknown diabetes.

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Results: Prevalence of pre-diabetes, unknown diabetes and known diabetes was 20.86, 3.37 and 4.39%, respectively. The correlations between HbA_{1c} and fasting glucose were higher than those obtained for HbA_{1c} and glycemia at 2 h of the oral glucose overload (0.344 and 0.270, respectively). Taking glucose levels as the gold standard, a greater discriminatory capacity was obtained for HbA_{1c} (area under de cruve: 0.839, 95% confidence intervals: 0.788–0.890). Based on the study criteria, the optimal minimum and maximum HbA_{1c} values were 5.9% and 6.7%, respectively.
Conclusions/interpretation: HbA_{1c} did not prove superior to glycemia for diagnosis of diabetes in the adult Galician population, and cannot therefore be used to replace the oral glucose tolerance test for screening and diagnosis purposes. Indeed, determination of glucose is essential to verify the diagnosis in the majority of cases.

PALABRAS CLAVE
HbA_{1c};
glucosa;
puntos de corte óptimos de la HbA_{1c}

Relación entre hemoglobina glucosilada y concentraciones de glucosa en la población gallega adulta: selección de los puntos de corte óptimos de la hemoglobina glucosilada como herramienta diagnóstica de la diabetes mellitus

Resumen
Objetivos/hipótesis: Analizar la relación entre la glucosa y la hemoglobina glucosilada (HbA_{1c}) en la población gallega adulta, evaluar el uso de la HbA_{1c} para cribado y diagnóstico de la diabetes y calcular el umbral diagnóstico necesario para este fin.
Métodos: Se analizaron datos de 2.848 sujetos (de 18–85 años de edad) procedentes de un estudio emprendido en 2004 para valorar la prevalencia de diabetes en Galicia. A efectos del estudio, se definió la diabetes de acuerdo con los criterios recomendados en 2002. Se clasificó a los participantes en cuatro grupos en función de los valores de glucosa. Se describió la relación entre glucosa y HbA_{1c} mediante modelos de regresión lineal, modelos aditivos generalizados y la correlación de Spearman. Se valoró la capacidad diagnóstica y se calcularon los puntos de corte óptimos de la HbA_{1c} como marcador de la diabetes empleando la curva de características operativas del receptor.
Resultados: Las tasas de prevalencia de prediabetes, diabetes desconocida y diabetes conocidas eran del 10,86, 3,37 y 4,39%, respectivamente. Las correlaciones entre la HbA_{1c} y la glucemia en ayunas eran mayores que las obtenidas entre la HbA_{1c} y la glucemia en ayunas dos horas después de la sobrecarga oral de glucosa (0,344 y 0,270, respectivamente). Tomando los valores de glucosa como referencia, se obtuvo una mayor capacidad discriminatoria para la HbA_{1c} (área bajo la curva: 0,839, intervalos de confianza del 95%: 0,788–0,890). Basándose en los criterios del estudio, los valores óptimos mínimos de la HbA_{1c} eran del 5,9 y el 6,7%, respectivamente.
Conclusiones/interpretación: La HbA1c no fue superior a la glucemia para el diagnóstico de la diabetes en la población gallega adulta, por lo que no puede utilizarse en lugar de la prueba de tolerancia oral a la glucosa con fines de cribado y diagnóstico. De hecho, la determinación de la glucosa es esencial para confirmar el diagnóstico en la mayoría de los casos.

Introduction

Ascertaining the prevalence of diabetes is important because it is a disease that is becoming increasingly prevalent.[1] Fasting glucose (FPG) and glycemia at 2 h after an oral glucose overload test (2hOGTT) were classical and now also glycated hemoglobin (HbA_{1c}) are used for diagnosis of diabetes. Although considered the ''gold standard'' for diagnosis, measurement of blood glucose is subject to several limitations as patient must fast at least 8 h, it has a large biological variability, samples are not stable, numerous factors alter glucose concentrations (diurnal variation, sample source, acute illness or stress), and it reflects glucose homeostasis at a single point in time.[2]

HbA_{1c} has advantages including its familiarity to clinicians, convenience, preanalytic stability, and assay standardization. It displays none of the variability inherent in the determination of glucose, it gives a better reflection of chronic hyperglycemia, and its concentration predicts the development of microvascular complications of diabetes.[2,3] HbA_{1c} has a number of limitations: may be altered by factors other than glucose (e.g., change in erythrocyte life span, ethnicity), some conditions interfere with measurement (e.g., selected hemoglobinopathies), it may not be available in some laboratories/areas of the world and its cost is higher than glucose determination.[2]

HbA_{1c} cut-off point has been set at $\geq$6.5% for diagnosis and at 5.7–6.4% for the diabetes high risk category.[4] The question arises, however, as to whether HbA_{1c} identifies the same population as does glucose. Accordingly, the aim of this study was to analyze the relationship between glucose and HbA_{1c} in the adult Galician population, and evaluate