Characterization of HbA1c Levels in a Subsample of Hispanic Adults Living in the San Juan Metropolitan Area

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Objective: To determine the mean levels of glycated hemoglobin (HbA1c) in a subsample of non-diabetic Hispanic Puerto Ricans living in the San Juan metropolitan area (SJMA) and to assess the sensitivity and specificity of HbA1c as a diagnostic test for prediabetes.

Research design and Methods: This was a secondary data analysis of the parent study, Burden of Diabetes and Hypertension in the Adult Population of the San Juan Metropolitan Area of Puerto Rico. Based on their HbA1c and fasting plasma glucose (FPG) values, 370 adults (147 males; 223 females) were classified as non-diabetics. An additional analysis of sensitivity, specificity, and predictive values for this subsample examined the association between FPG and HbA1c.

Results: The mean HbA1c among the non-diabetic population was 5.38% (±0.23). Sensitivity, specificity, and the area under the receiving operating characteristic curve were 56.8%, 74.2%, and 84.3%, respectively, for the diagnosis of prediabetes, using HbA1c as the sole diagnostic test (P<0.001).

Conclusion: This study demonstrated that HbA1c levels among the non-diabetic Hispanic population residing in the SJMA were very similar to those of non-Hispanic whites living in the US. Our results are consistent with those of other studies that have shown that the sensitivity of the HbA1c test is too low to be used in the diagnosis of prediabetes. [*P R Health Sci J 2018;37:78-82*]

Key words: HbA1c, Glycated hemoglobin, Hispanics

Glycated hemoglobin (HbA1c) was first recognized as a useful tool for diabetes management over 20 years ago. Nathan et al. compared the clinical value of HbA1c against other forms of diabetes monitoring and found that HbA1c had a linear correlation with the daily self-monitoring of blood glucose and was useful as a method for assessing mean glucose levels over a period of time (1). In 2008, an international committee of experts, the members of which were selected by the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), and the International Diabetes Federation (IDF), recommended the use of HbA1c as a method for diagnosing diabetes mellitus (DM) (2). The HbA1c cutoff value of 6.5% for the diagnosis of DM was selected because of the higher prevalence of diabetic retinopathy observed at and above this value (2–3). The cutoff value selected by the committee mentioned above for the diagnosis of prediabetes was the HbA1c level of 5.7% (2).

In recent years, a debate has arisen regarding possible ethnic and regional variations in the baseline levels of HbA1c and the observed complications in DM seen at already established cutoff values (3, 4). Recent studies have reported differences in HbA1c levels that are linked to ethnicity (3, 4). In addition, it has been found that complications from diabetes can occur at levels below previously established HbA1c diagnostic guidelines (3–4). Cohen found a difference of 0.2% to 0.4% higher HbA1c values in African Americans compared to whites (4). This difference was also observed in a review of the 1999–2000 National Health and Nutrition Examination Survey (NHANES), which showed higher mean HbA1c levels in diagnosed and undiagnosed blacks than in whites with diabetes (8.1% vs 7.6%) (5).

Variations in HbA1c levels have also been reported in the Latino community living in the US (6–7). These differences have led some authors to propose ethnicity-specific HbA1c cutoff points for the diagnosis of DM (8–9).

In a recent investigation, using the ADA cutoff points, Allende et al. estimated the prevalence of type 2 DM to be 15.2% in

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adults residing in the San Juan metropolitan area (SJMA) of Puerto Rico (10). In another study, Pérez and colleagues found that the mean HbA1c level in adults residing in the SJMA was 6.3% (11). Given that the population of Puerto Rico consists of an admixture of different genetic characteristics, the aim of the current study was twofold: to describe the distribution and mean levels of HbA1c and fasting blood glucose (FPG) in a subsample of Puerto Rican adults with normoglycemia and prediabetes; and to assess the diagnostic accuracy of HbA1c for predicting prediabetes, using FPG as the standard.

Study design

This is a secondary data analysis of the parent study *Burden of Diabetes and Hypertension in the Adult Population of the San Juan Metropolitan Area of Puerto Rico* (10). The study population consisted of a sample of non-institutionalized Puerto Ricans residing in the SJMA. According to the 2010 Census, there were 955,431 inhabitants aged 18 to 79 years in this geographical area, which consists of 7 municipalities: Carolina (n = 152,396), Trujillo Alto (n = 65,732), San Juan (n = 347,065), Guaynabo (n = 86,746), Bayamón (n = 195,814), Toa Baja (n = 82,418), and Cataño (n = 25,260). A sample of 450 Puerto Ricans aged 18 to 79 years residing in the SJMA was recruited using a complex, multistage, probability sampling method. Further details about the sampling method and study design have been published elsewhere (10). This study was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus. Informed consent was obtained from all the subjects prior to their participation in the study.

Inclusion and Exclusion criteria

Only subjects with normoglycemia (defined as an FPG below 100 mg/dL and HbA1c below 5.7%) or prediabetes (defined as an FPG from from 100 to 125 mg/dL and/or HbA1c from 5.7% to 6.4%) were included in this secondary data analysis. This subsample included 370 subjects 147 men and 223 women from 18 to 79 years of age, living in the SJMA.

Statistical analysis

Descriptive statistics were used to summarize the socio-demographic characteristics of the study group. A contingency table was used to describe the classification of participants based on FPG and HbA1c measurements. Scattergram plots were used to describe the linear relationships between HbA1c and age and between HbA1c and FPG levels. Simple linear regression models were constructed to assess the significance of these relationships. Coefficients of determination and Pearson correlations were estimated to assess the magnitude and direction of these relationships. We assessed the sensitivity and specificity of HbA1c in the diagnosis of prediabetes, using FPG as the gold standard. The receiver operating characteristic (ROC) curve for HbA1c for the detection of prediabetes by FPG was used to compute the area under the curve (AUC) for estimating the probability of correctly identifying subjects with prediabetes. An AUC of 0.5 in the ROC curve corresponds to random chance and an AUC of 1.0 to perfect accuracy (Figure 4). All the statistical analyses were performed using the statistical package Stata, version 13 (12).

Results

The study group was composed of 370 participants (147 males and 223 females) who were classified as non-diabetics. Participants over 50 years old made up 44.3% of the sample; 50.8% reported having more than 12 years of education, and 13.5% reported having no health insurance (Table 1). Of the subjects classified as having normal FPG levels, 74.2% also had normal HbA1c levels. However, only 56.8% of the subjects categorized as having prediabetes based on their FPG levels would be similarly categorized based on their HbA1c levels (5.7%–6.4%) (Table 2).

Table 1. Baseline characteristics of study participants (n = 370)

	Frequency	%
Gender		
Male	147	39.7
Female	223	60.3
Body mass index (BMI), kg/m^2		
<18.5	11	2.9
18.5–24.9	85	23.10
25–29.9	127	34.1
≥ 30.0	145	39.40
Age (years)		
<50	206	55.7
≥ 50	164	44.3
Smoked		
Yes	225	60.8
No	144	39.0
Refused to answer	1	00.2
Education (years)		
<8	42	11.4
9–12	140	37.8
>12	188	50.8
Annual family income		
<$ 20,000	210	56.7
$20,000–$50,000	96	26.0
>$50,000	23	06.2
Refused to answer	41	11.1
Primary medical insurance		
Private	195	52.7
Public	125	33.8
None	50	13.5
Marital status		
Single	96	25.9
Legally married	143	38.7
Other	131	23.4

HbA1c values were highly concentrated in the highest range (Figure 1). The mean level of HbA1c among those classified as non-diabetics was 5.38% (±0.23). The linear relationship between HbA1c and age showed a significant association ($p<0.05$), with 28% of the variability of HbA1c explained by

this model (Figure 2). In addition, a significant relationship was found between HbA1c and FPG (p<0.05), with 26% of the variability of HbA1c explained by this model (Figure 3). We assessed the sensitivity and specificity of HbA1c in the diagnosis of prediabetes. A sensitivity of 56.8% and specificity of 74.2% were found. The positive and negative predictive values of HbA1c were 22.2% and 94.2%, respectively. The area under the ROC analysis was 0.84 (95% CI: 0.78, 0.89) (Figure 4). However, when the analysis was stratified by age group (≤ 45 years vs. >45 years) and HbA1c group (≤ 5.7% vs. >5.7%), the AUC of subjects over 45 years of age and having an HbA1c over 5.7% reached only 0.72 (95% CI: 0.60, 0.83) in terms of being able to correctly categorize the subjects with prediabetes.

Table 2. Cross-tabulation of the classification of participants based on FPG and HbA1c measurements (n = 370)

FPG	HbA1c <5.7% (normal) n (%)	HbA1c 5.7%–6.4% (prediabetes) n (%)	Total
<100 mg/dl (normal)	242 (74.2%)	84 (25.8%)	326
100–125 mg/dl (prediabetes)	19 (43.2%)	25 (56.8%)	44
Total	261 (70.5%)	109 (29.5%)	370

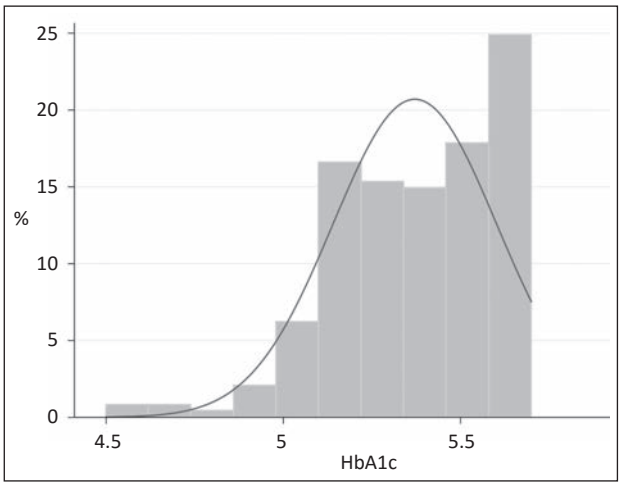

Figure 1. HbA1c distribution among participants classified as non-diabetics, based on FPG and HbA1c measurements

Discussion

Recent studies suggest that the value of HbA1c is affected by the race/ethnicity of a population, with discrepancies in mean HbA1c percentages among whites, blacks, and Hispanics (5–7). It has been established that HbA1c levels can be affected by shortened red-cell survival, mutations at the hemoglobin structural level and systemic conditions such as liver or kidney disease, and iron deficiency anemia (13). In the Diabetes Prevention Program study, mean levels of HbA1c in patients with impaired glucose tolerance were analyzed among different ethnic groups, showing that compared to other ethnic groups, whites had the lowest HbA1c levels (5.80% ± 0.44)

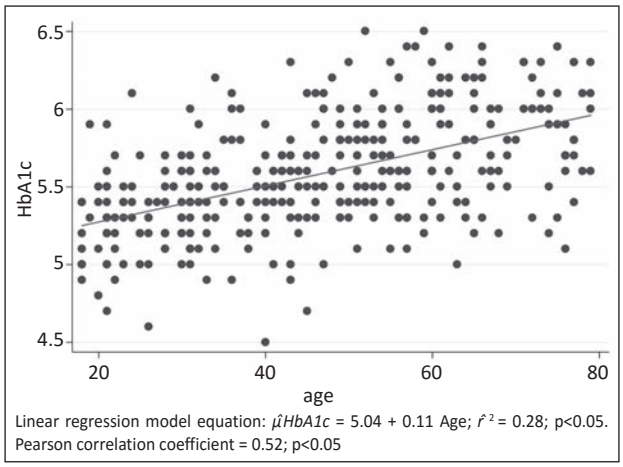

Figure 2. Relationship between HbA1c levels and age among participants classified as non-diabetics, based on FPG and HbA1c measurements.

and blacks had the highest levels (6.19% ± 0.59) (14). Some studies have proposed that this difference is due to health care disparities. However, studies of organized health care systems continue to report this difference between the 2 populations (13–16).

This difference in HbA1c levels has also been explored in non-diabetic populations. The analysis of the Atherosclerosis Risk in Communities study (ARIC), Selvin and colleagues showed a significant difference in HbA1c levels between whites and blacks (5.4% vs. 5.8%; p<0.001) (16). In our study group, the estimated mean level of HbA1c (5.38%) was similar to the reported mean level for whites in the US (16–17). In a sub-analysis of the NHANES 2005–2010, Menke et al. found a statistically significant difference in the mean levels of HbA1c of different groups, with a mean HbA1c of 5.7% in the Mexican-American population, 5.8% in non-Hispanic blacks, and 5.5% in non-Hispanic whites (18). Ziemer et al. also found a significant difference in HbA1c levels between blacks and whites (5.7% ± 0.04 vs. 5.5% ± 0.02; p<0.001) (17).

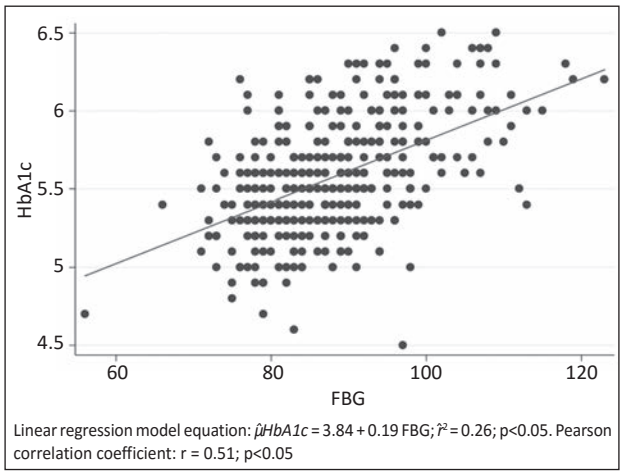

Figure 3. Relationship between HbA1c and FPG levels among participants classified as non-diabetics

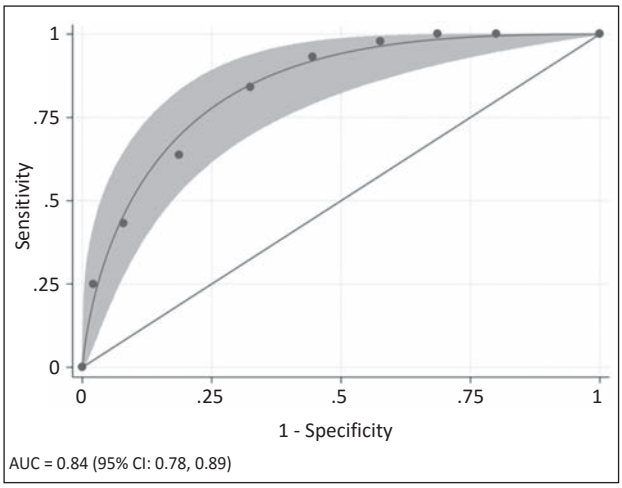

Figure 4. Receiver operating characteristic curve for HbA1c for detection of prediabetes, by FPG

Our results indicate that an HbA1c lower than 5.7% is strong evidence that prediabetes should be ruled out, but in view of the low sensitivity of HbA1c values from 5.7% to 6.4%, most of the affected subjects were not classified as having prediabetes, per current guidelines (19). This type of misclassification could delay early therapy and could contribute to the progression of long-term complications of diabetes in this specific group of patients. Mann et al. found that the combined use of HbA1c and FPG to diagnose prediabetes would be more sensitive, in comparison to using FPG or HbA1c alone, but such use would eliminate the advantage of using HbA1c as the only test (20). It is well known that HbA1c has significant practical advantages over FPG, since the test is more stable and the subject does not have to fast prior to testing. It has become the preferred method among physicians for diagnosing diabetes and prediabetes. If HbA1c were to be used as the sole means of diagnosing DM, this could have a clinical impact, as a large subgroup of patients who previously would have been classified as prediabetics by FPG would now be excluded, leading to a delay in their diagnosis and treatment. It is important to consider not only the practicality but also the adequacy of the method as well as the length of time necessary when diagnosing DM, a condition with multiple comorbidities that can be delayed or prevented if treated in the early stages of the disease. Several limitations of this study must be taken into consideration. Our results cannot be generalized to the entire population of the SJMA (21) since the sample was small. Because of that small sample size, associations between body weight and prediabetes could not be analyzed. Furthermore, we did not use a glucose tolerance test to define prediabetes, nor did we collect data on hematological conditions or any other factor that might affect HbA1c values. Despite these limitations, this is the first study to demonstrate that HbA1c levels in non-diabetic Hispanic Puerto Ricans are similar to those of whites on the US mainland.

After our work was submitted for publication, the findings of our study were confirmed. Published in 2016, an analysis by the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) reported that the FPG and HbA1c tests were found not to be sensitive, though they were highly specific in terms of detecting probable DM among Hispanics/Latinos, independent of their specific racial or ethnic heritage (22). This is in accordance with the findings in our study. In another analysis of data from the HCHS/SOL, Avilés-Santa et al. concluded that the HbA1c test alone was a poor test for use in the diagnosis of prediabetes due to its low sensitivity, which finding is in accordance with that of our study (23). In this analysis, FPG and HbA1c together were more sensitive at detecting prediabetes than was either test alone. The population of the HCHS/SOL study includes 15.6% who are of Puerto Rican heritage. In a study published in 2017 by Vega-Vázquez et al., a low concordance rate was observed between HbA1c and glucose measurements (24). The authors concluded that HbA1c is not a good test for prediabetes, a similar finding to what was discovered by our study. The participants recruited for this study, the San Juan Overweight Adults Longitudinal Study, were obese, the majority of them were Hispanic (98%). The A1c levels in this study of Hispanic/Puerto Ricans were also similar to those of mainland whites (5.3%). The analyses of both the HCHS/SOL and the NHANES (2007–2012) showed that non-Hispanic whites had significantly lower HbA1c levels ($P<0.05$) than did the individuals having Hispanic/Latino heritage, including the 15.6% who had specifically Puerto Rican heritage (25). This study had a large sample size and found similar HbA1c levels in non-diabetic Hispanic/Puerto Ricans and whites on the US mainland (5.35%), which is similar to what we found.

Conclusions

Although the Hispanic population in Puerto Rico has a multiracial background, the mean HbA1c level of the non-diabetic study group appears to be similar to non-Hispanic whites living in the US. In line with previous studies, we found poor agreement in the consistency between HbA1c and FPG criteria in classifying prediabetes. Due to the high prevalence of prediabetes and diabetes in our population, additional strategies for identifying individuals with impaired glucose tolerance must be assessed in order to design strategies for optimal medical care, particularly in the prevention and treatment of type 2 diabetes.

Resumen

Objetivo: Determinar el nivel promedio de hemoglobina glucosada (HbA1c)en una sub-muestra de población no diabética hispana residente en el área metropolitana de San Juan (SJMA) y evaluar la sensibilidad y especificidad de la HbA1c como medida diagnóstica. Métodos y Diseño de Investigación: Este es un análisis secundario de los datos del estudio "Burden of Diabetes and Hypertension in the adult population of the San Juan Metropolitan Area of Puerto Rico". Basado en valores de HbA1c y FPG, 370 adultos (147 hombres, 223 mujeres) se

clasificaron como no-diabéticos. Se analizó la asociación entre HbA1c y FPG analizando valores de sensibilidad, especificidad y valores predictivos. Resultados: El promedio de HbA1c de la población no diabéticos fue 5.38%±0.23. La sensibilidad, especificidad y el área bajo curva característica operacional fueron 56.8%, 74.2% y 84.3%, respectivamente, para el diagnóstico de prediabetes utilizando HbA1c como única prueba diagnóstica (P <0.001). Conclusión: Este estudio demuestra que el nivel promedio de HbA1c en población no diabética residente de SJMA es similar a los blancos no hispanos que viven en los Estados Unidos. Nuestros resultados son congruentes con otros estudios que han demostrado una baja sensibilidad de la prueba de HbA1c para el diagnóstico de prediabetes.

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