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COMPARING GLUCOSE AND HEMOGLOBIN A_{1c} DIAGNOSTIC TESTS AMONG A HIGH METABOLIC RISK HISPANIC POPULATION

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Abstract

AIMS—Compare HbA_{1c} diagnostic tests for pre-diabetes and diabetes with plasma glucose criteria (PGC), and compare the metabolic profiles of people classified by HbA_{1c} versus by glucose levels.

METHODS—Participants were recruited for the San Juan Overweight Adults Longitudinal Study (SOALS). Were primarily Hispanic (98%), without previously diagnosed diabetes, and aged 40–65 years. Participants classified as normal glycemic, pre-diabetes or diabetes based on baseline HbA_{1c} and PGC, were compared with respect to baseline cardiometabolic factors.

RESULTS—The 1,342 participants had a mean age of 50.5±6.8 and 28% were men. Thirty-one percent were diagnosed with pre-diabetes by PGC and 53.4% by HbA_{1c}, 8.1% were diagnosed with diabetes by PGC and 6.3% by HbA_{1c}; overall concordance rate was 55.1%. The area under the ROC curve (AUC) of HbA_{1c} compared to PGC was 0.62 for impaired glucose and 0.76 for diabetes. A worse cardiometabolic profile was seen within subgroups that met HbA_{1c} and PGC criteria for diabetes or pre-diabetes. Those diagnosed with pre-diabetes by PGC had significantly higher systolic blood pressure and higher HOMA than those diagnosed using HbA_{1c}. Participants diagnosed with diabetes by PGC had lower BMI, smaller waist circumference, lower insulinogenic and disposition indices, but higher HOMA-IR, than those diagnosed by HbA_{1c}.

CONCLUSIONS—Low concordance was seen between HbA_{1c} and glucose tests. The HbA_{1c} is not a good test for pre-diabetes, but shows reasonable validity for diabetes in this high-risk

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Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

predominantly female Hispanic population. People classified by HbA_{1c}, PGC, or both show different metabolic profiles; a combined test may be ideal.

Keywords

diabetes; diagnosis; ethnicity; HbA_{1c}; IGT

Introduction

Type 2 diabetes accounts for almost 90% of the population with diabetes, and includes individuals who have insulin resistance and who usually develop relative insulin deficiency. The prevalence of diabetes varies by racial/ethnic groups. Among ethnic groups, Hispanics have among the highest risks for developing type 2 diabetes, second only to African-Americans [1].

For decades, the diagnosis of diabetes was based on plasma glucose criteria (PGC), either with the fasting plasma glucose (FPG) or the 2-hour value in the oral glucose tolerance test (OGTT) [1,2]. Diagnostic criteria for diabetes using glucose values include a FPG ≥ 7.0 mmol/L, and a 2-hour plasma glucose ≥ 11.1 mmol/L during the OGTT. It was not until 2009, that the International Expert Committee on Diagnosis and Classification of Diabetes Mellitus recommended the use of the glycated hemoglobin (HbA_{1c}) test to diagnose diabetes with a threshold of ≥ 48 mmol/mol (6.5%) [1,3]. The Committee also recognized an intermediate group of patients with increased risk for diabetes, known as pre-diabetes, as described below.

Diabetes prevalence is increasing worldwide [4], and it is important to study the diagnostic accuracy of HbA_{1c} and its relationship with other important metabolic and clinical parameters. Even though some reports propose that HbA_{1c} is useful as a diagnostic criterion of diabetes [1–3,5–6], others suggest that its diagnostic usefulness is inferior to standard testing because of a low sensitivity [7–12]. Given the HbA_{1c} variability among different racial/ethnic groups, its value as a diagnostic tool for diabetes in high-risk populations has been the source of great debate [13–14]. The early identification of subjects at high risk for diabetes offers the opportunity to develop tools that may prevent or delay the progression of the disease, and reduce the complications associated with this chronic condition and its burden to society.

This study assesses the value of HbA_{1c} as a diagnostic criterion for impaired glucose metabolism and to assess its concordance with the PGC results among a high metabolic risk population. We also describe and compare the metabolic characteristics and risk factors that may differ between participants with altered PGC and/or HbA_{1c} in the context of other clinical diagnoses associated to cardiovascular and renal function.

Patients and Methods

Study Population

This is a cross-sectional analysis of 1,342 participants, free of diagnosed diabetes that were recruited for the San Juan Overweight Adult Longitudinal Study (SOALS). The SOALS is a

cohort study designed to evaluate the bidirectional association between pre-diabetes and periodontal disease. Individuals were recruited from around the San Juan Metropolitan area through press releases, advertisements, flyers and word of mouth. The eligibility criteria include: (1) age between 40 and 65 years and (2) overweight or obese. Most of the exclusion criteria relate to health conditions that could potentially increase the risk of systemic complications from the periodontal exam, which was a key component of SOALS. The exclusion criteria were the following: (1) diagnosis of diabetes mellitus or taking insulin or oral anti-diabetic agents prior to the baseline exam, (2) less than four natural teeth, (3) metastatic cancer and/or undergoing cancer related treatment, (4) having braces or orthodontic appliances, (5) pregnancy, (6) physician-diagnosed hypoglycemia, congenital heart murmurs, heart valve disease, congenital heart disease, endocarditis, rheumatic fever, hemophilia or bleeding disorders, (7) active dialysis treatment, (8) active anticoagulant therapy, (9) prescribed antibiotic prophylaxis prior to surgical or dental procedure, (10) having undergone procedures related to cardiovascular disease, (11) having undergone hip bone or joint replacement surgery, (12) severe health conditions or psychological or physical disabilities, (13) plans for moving away in the next three year period. In addition, for this analysis, we excluded 9 participants who were missing OGTT results. Participants signed informed consents.

Measurements

Participants were asked to fast for 10 hours prior to their appointment, and up to the conclusion of the last blood drawing. Fasting blood was drawn for baseline glucose, insulin, HbA_{1c}, C-reactive protein (hs-CRP) and serum lipids levels. Blood glucose was evaluated at 30-min, 1-hour and 2-hour after the consumption of a glucose drink containing 75 grams dextrose.

We calculated the homeostatic model assessment of insulin resistance (HOMA-IR) [15], and the insulinogenic index $[(30 \text{ minutes insulin} - \text{fasting insulin}) \div (30 \text{ minutes glucose} - \text{fasting glucose})]$. The disposition index $(\text{HOMA}_{\text{IR}} \div \text{insulinogenic index})$ was calculated to estimate pancreatic β cell insulin secretory capacity.

Interviews were conducted to collect sociodemographic variables, health-related habits and medical history. Weight, height and waist and hip circumferences, were collected and BMI was calculated. Blood pressure was assessed using standard procedures.

Participants were stratified into categories for normal glycaemia (NG), pre-diabetes and diabetes according to the results of the PGC and HbA_{1c} level based on the current American Diabetes Association recommendations [1]. For HbA_{1c}, the cutoffs for pre-diabetes and diabetes are 48 mmol/mol (5.7%) and 62 mmol/mol (6.5%), respectively. In terms of the PGC, the cutoffs for pre-diabetes are 5.5–6.9 mmol/L for fasting glucose and 7.8–11 mmol/L for 2 hour glucose, and for diabetes, fasting glucose ≥ 7.0 mmol/L and 2 hour glucose ≥ 11.1 mmol/L.

Statistical analysis

Statistical analysis was done using the software Stata 13.1. Continuous variables were presented as the mean $\pm$ standard deviation and categorical data as percentages. To

investigate whether the method used for diagnosing impaired glucose metabolism identifies individuals with different metabolic characteristics, the study population was stratified into concordant and discordant subgroups within the pre-diabetes and diabetes categories. To compare subgroups with different combinations of diabetes status classification by PGC or HbA_{1c}, we used t-test. Using the PGC as the gold standard, the diagnostic value for HbA_{1c} was assessed for specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV); accuracy was assessed by the area under the receiver operating characteristic (ROC) curve (AUC) for impaired glucose metabolism and diabetes. Confidence intervals (CI) and p-values were calculated. The Kappa statistic was calculated to assess how PGC and HbA_{1c} classified participants as with diabetes or with pre-diabetes. Logistic regression analyses (adjusted for age, sex, BMI and waist circumference) were used to study the association of glucose tolerance categories according to PGC or HbA_{1c} with insulin resistance (HOMA-IR > 4th quartile of NGT participants), insulin secretion (Insulinogenic Index < 1st quartile of NG participants) and β cell function (using the Disposition Index < 1st quartile of NG participants). Odds ratios and 95% CIs are presented for adjusted models.

Results

The sample consisted of 1,342 participants (71.8% women, 28.2% men). The mean age of this study population was 50.5 ± 6.8 years with BMI of 33.4 ± 6.2 kg/m² and HbA_{1c} level of 40 ± 7.7 mmol/mol ($5.8 \pm 0.7\%$). Table 1 presents the population profile.

When the NG group was compared against the pre-diabetes group with concordant diagnostic criteria (i.e. ⁺PGC/⁺HbA_{1c}), we observed that the pre-diabetes concordant group was significantly older (52.4 vs. 48.6 years; $p < 0.0001$), had higher BMI (34.6 vs. 32.1 kg/m²; $p < 0.0001$), had significantly larger waist circumferences (males, 107.0 vs. 115.7 cm, $p = 0.0001$; females, 102.1 vs. 106.7 cm, $p < 0.0001$), systolic blood pressure (131.8 vs. 125.6 mmHg; $p < 0.0001$), diastolic blood pressure (82.4 vs. 79.8 mmHg; $p = 0.0005$) and had a significantly worse lipid profile, with higher triglycerides and LDL levels and lower HDL levels. This concordant group with pre-diabetes also had significantly higher hs-CRP levels (64.0 vs. 45.2 nmol; $p < 0.0001$) and had higher HOMA-IR levels (3.5 vs. 1.9; $p < 0.0001$), than the NG group. In the group with pre-diabetes, those fulfilling only one of the criteria for diagnosis were compared (⁺PGC/⁻HbA_{1c} vs. ⁻PGC/⁺HbA_{1c}); those in the category of ⁺PGC/⁻HbA_{1c} for pre-diabetes had significantly higher age, BMI, waist circumference, fasting insulin, Insulin Sensitivity Index, Disposition Index, higher diastolic blood pressure (82.4 vs. 80.5 mmHg, $p = 0.04$), more insulin resistance (HOMA-IR: 3.5 vs. 2.8; $p = 0.0007$) and lower HDL (1.2 vs. 1.3 mmol/L; $p = 0.04$).

The same analysis was performed for participants in the group diagnosed as having diabetes by any criteria. The concordant group for diabetes was significantly older (51.5 vs. 48.6 years; $p = 0.0009$), had higher BMI (34.3 vs. 32.1 kg/m²; $p = 0.002$), larger waist circumference (111.8 vs. 103.4 cm; $p < 0.0001$) and higher systolic and diastolic blood pressure readings when compared to the concordant NG group. We also found higher total cholesterol levels (5.3 vs. 5.0 mmol/L; $p = 0.02$), higher triglycerides (2.4 vs. 1.5 mmol/L; $p < 0.0001$) and lower HDL levels (1.2 vs. 1.3 mmol/L; $p = 0.002$), although no difference in

LDL levels. This concordant group for diabetes had significantly lower insulinogenic index, higher inflammatory markers (hsCRP) and higher HOMA-IR levels than the NG concordant group. In the group of subjects with diabetes fulfilling only one criteria for diagnosis (i.e. $^{+}PGC/-HbA_{1c}$ and $^{-}PGC/+HbA_{1c}$), those with $^{+}PGC/-HbA_{1c}$, had lower BMI (32.9 vs. 36.5 kg/m²; $p = 0.02$), smaller waist circumference (107.7 vs. 113.5 cm; $p = 0.03$); and lower insulinogenic index (0.34 vs. 0.72; $p = 0.01$) and a lower disposition index (0.07 vs. 0.22; $p = 0.02$) were also found in this group, reflecting a more impaired insulin secretion and worse pancreatic β -cell function than those with $^{-}PGC/+HbA_{1c}$ for diabetes.

Using only the PGC to stratify our cohort, we found that 60.6% were classified as NG, 31.3% had pre-diabetes and 8.1% were identified with diabetes. Meanwhile, stratifying by HbA_{1c} levels, only 40.2% of the participants were classified as NG, 53.4% had pre-diabetes and 6.3% had diabetes. In our study, HbA_{1c} failed to identify 46.8% of the participants classified with diabetes as per PGC. Of the participants classified with pre-diabetes by the PGC, 66.2% of the subjects were also identified as such by the HbA_{1c}, 29.5% were misclassified as NG and 4.3% were misclassified as having diabetes. Among the subjects with diabetes by PGC, 11.9% were classified as NG and 34.9% were classified as pre-diabetes by the HbA_{1c} criteria (Table 2).

Using PGC as the gold standard, the specificity and sensitivity of HbA_{1c} as per the current recommended cutoff for impaired glucose metabolism (pre-diabetes) were 49.6% and 74.1%, respectively. For diabetes, the specificity and sensitivity of HbA_{1c} was 97.8% and 53.2% respectively. The positive predictive value of HbA_{1c} for pre-diabetes was 48.9, and for diabetes 68.2. Fig 1 shows ROC curves of HbA_{1c} compared to OGTT. The AUC was 0.62 (95% CI 0.59–0.64, $p < 0.001$) for impaired glucose metabolism; it increased to 0.67 after controlling for age, gender and smoking. For diabetes the AUC was 0.76 (95% CI 0.71–0.80, $p < 0.001$), and it increased to 0.80 after controlling for age, gender and smoking. However the overall agreement between PGC and HbA_{1c} criteria was 55.1%. Kappa for diabetes was 0.57 and for pre-diabetes was 0.22. To investigate whether the percent agreement between the PGC and HbA_{1c} varies according to weight, the population was stratified among overweight and obese participants. The overall percent agreement of the tests remaining similar, among overweight it was 56.4% and 54.3% for the obese subjects.

Logistic regression analysis adjusted for age, sex, BMI and waist circumference showed that participants classified with pre-diabetes and diabetes by PGC only, had a higher likelihood of insulin resistance and greater impairment in insulin secretion (Table 3) than those diagnosed by HbA_{1c} criteria only.

Discussion

In this high metabolic risk population, we studied two different and internationally validated diagnostic tests to identify diabetes and pre-diabetes. We found that the agreement between the two tests was low, which is consistent with previous reports in other populations [8,16–18]. Discordance between the HbA_{1c} and glucose tests is somewhat expected, given the different metabolic processes that are captured by each one. The AUC at 0.62 for impaired glucose suggests that the HbA_{1c} is not a good test to classify the subjects as pre-diabetics;

however the 0.76 area under the ROC curve for diabetes shows reasonable validity for this population.

The HbA_{1c} was first described in the late 1960's, as a glycated form of hemoglobin that was elevated in patients with diabetes [19]. It has several advantages to the FPG and OGTT, including greater convenience, evidence to suggest greater pre-analytical stability, and less day-to-day perturbations during periods of stress, high glucose load and illness, as it reflects average glycaemia over several months [2]. Several studies have also shown a strong predictive value of HbA_{1c} for diabetes complications [3]. Since the lifespan of erythrocytes is constant and erythrocytes are freely permeable to glucose, hemoglobin glycation occurs non-enzymatically at a rate directly proportional to the ambient glucose concentration; hence, HbA_{1c} provides a glycaemic history of the previous 120 days [13]. However, our results show that the HbA_{1c} has low concordance with glucose criteria. The specificity and sensitivity were low for identifying pre-diabetes, and, for identifying participants with diabetes, it was found to be a specific but insensitive method. These findings are in agreement with those reported by other authors [8]. The HbA_{1c} has several limitations for the diagnosis of diabetes; conditions that affect erythrocyte turnover, such as hemolysis or blood loss, hemoglobin variants, structural hemoglobinopathies or erythropoietin therapy will affect the test results. The potential magnitude of this problem depends also on the prevalence of hemoglobinopathies, which may vary across different races and ethnicities. Advanced liver disease, kidney disease and iron deficiency have also been reported to impact HbA_{1c} test results [5]. In addition, racial and ethnic differences in the relationship between HbA_{1c} and blood glucose have been described [13–14]. Factors such as variations in red cell survival, extracellular-intracellular glucose balance and non-glycaemic genetic determinants of hemoglobin glycation have been explored as contributors to these disparities [13].

It has also been reported that the oxidative stress, which has been shown to be higher among overweight and obese subjects [20], might also play an important role during the glycation process of hemoglobin [21–23] and it may somehow explain the discordance among these tests independently of the glucose concentration environment [21]. Moreover, Li et al. found that the agreement between HbA_{1c} criteria and OGTT can be affected by BMI, and it can be significantly improved by shifting the HbA_{1c} threshold for pre-diabetes within the obese population [21]. Although oxidative stress biomarkers were not measured in our study and their role during the glycation process of hemoglobin is still uncertain, when we stratified our population by overweight and obese, the percent of agreement among the tests did not change dramatically among the subgroups.

Not surprisingly and similarly to findings reported by Bianchi et al. [8] and Boronat et al. [24], we found that the participants without impairment in glucose metabolism by both criteria had the most favorable cardiometabolic risk profile. In our study, participants with diabetes as per the HbA_{1c} criterion were found to have a higher BMI, larger waist circumference and a tendency toward lower HDL compared to those meeting only the PGC, supporting that HbA_{1c} levels might relate to the metabolic syndrome [24–25]. Moreover, participants with pre-diabetes and diabetes based only on the glucose criteria, were found to have more insulin resistance (i.e. had higher HOMA-IR) than those categorized by HbA_{1c} only; which could be explained by the muscle insulin resistance that characterizes impaired

glucose tolerance as described by Bianchi et al. [8] and Abdul-Ghani et al. [26]. Interestingly, among diabetics, the group diagnosed with both criteria had the highest proportion of males (45%), followed by the group diagnosed with only PGC (39%), and the group with HbA_{1c} only had only 11% males.

In our sample, those diagnosed as diabetics by both criteria, the HbA_{1c} was high (mean=8.2%, SD=1.6) suggesting that people with high levels detected from the study had not been diagnosed, and a large proportion of this population may have undetected diabetes.

Although a logistic regression analysis showed that individuals with pre-diabetes and diabetes classified by PGC had a greater probability to have insulin resistance and greater impairment in insulin secretion, it is important to recognize that these calculations are computed from indices derived from the fasting state and OGTT. However the more accurate hyperinsulinemic euglycaemic clamp tests may not be feasible in large epidemiologic studies.

The strengths of this study include a reasonably large sample size of overweight and obese adults, a standardized protocol for data collection and laboratory analyses, and the availability of both fasting plasma glucose levels and OGTT. There are a number of limitations to this study. Like in most clinical settings and research studies, participants were not tested for anemia, renal impairment or conditions that could result in abnormal red blood cell turnover, such as recent blood loss, blood transfusion or hemoglobinopathies. Another important limitation is that the blood samples were only taken once during the initial visit; thus, no re-testing was done for abnormal findings. The cross-sectional data limits our ability to compare the two tests with respect to eventual progression; however, the focus of this paper is on diagnosis. In order to address some of these limitations, we gather information about other clinical conditions that were self-reported by participants. Such preliminary analysis does not indicate that an over representation of health conditions other than diabetes would have introduced unforeseen bias in this study. Last, our study sample consists of 72% women and is not representative of the overall population; however men and women had similar AUC comparing HbA_{1c} with impaired glucose (0.63 vs. 0.62) and diabetes (0.78 vs. 0.74), and similar percent agreement for pre-diabetes/diabetes status (57.9 vs. 53.9). One can expect that these findings may be comparable to other overweight populations within a similar age range.

Several studies have compared the HbA_{1c} with FPG and OGTT for the detection of pre-diabetes and diabetes in different populations. Participants with isolated elevated glucose appear to be metabolically different from those with isolated elevated HbA_{1c}. Although the HbA_{1c} appears to be an attractive test given that it does not need fasting or repeated samples, and has lower day-to-day variation, its limited concordance with the glucose tests is of great concern. An early identification of individuals at high risk for developing diabetes (i.e. people with pre-diabetes) is extremely important in order to initiate early interventions that may prevent or delay the progression of this chronic dire condition. Our results in a high risk overweight, middle age, predominantly Hispanic population suggests that HbA_{1c} test has low specificity and sensitivity especially for the pre-diabetes diagnosis and may result in frequently missed or delayed diagnosis. Its performance in different populations, its use as a

sole screening or diagnostic tool, and the thresholds must be re-considered. Further longitudinal studies are needed to resolve the current controversy of using HbA_{1c} for diagnosing pre-diabetes and diabetes.

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Figure 1. Pre-diabetes and Diabetes Prediction of HbA1c compared to OGTT

(a) ROC curve for pre-diabetes prediction of HbA1c compared to OGTT (b) ROC curve for pre-diabetes prediction of HbA1c compared to OGTT adjusted for age, gender and smoking, (c) ROC curve for diabetes prediction of HbA1c compared to OGTT (d) ROC curve for pre-diabetes prediction of HbA1c compared to OGTT adjusted for age, gender and smoking.

Clinical parameters among subjects with normal plasma glucose and concordant and discordant groups for pre-diabetes and diabetes, using the plasma glucose criteria (PGC) and HbA_{1c}.

Table 1

Characteristics	NORMAL		PREDIABETES				DIABETES			
	A. NG	B. (+)PGC (+)HbA _{1c}	C. (+)PGC (-)HbA _{1c}	D. (-)PGC (+)HbA _{1c}	E. (+)PGC (+)HbA _{1c}	F. (+)PGC (-)HbA _{1c}	G. (-)PGC (+)HbA _{1c}			
n	403	278	142	439	58	51	27			
Age, years	48.6±6.4	52.4±7.0 [*]	50.6±6.9	50.9±6.6	51.5±6.5 [‡]	51.9±6.5	51.3±6.7			
Male Gender, n (%)	109 (27.1)	84(30.2)	54 (38.0)	99 (22.6) ^{**}	26 (44.8) [‡]	20 (39.2)	3 (11.1) ^{‡‡}			
BMI, kg/m ²	32.1±5.7	34.6±6.5 [*]	33.1±6.1	34.0±6.5	34.1±4.7 [‡]	32.9±5.9	35.8±6.6 ^{‡‡}			
Waist Circumference, cm (Male)	107.0±14.6	115.7±16.0 [*]	107.9±12.2	113.0±15.9 ^{**}	115.2±12.1 ^{***}	105.3±11.2	114.9±24.1 ^{****}			
Waist Circumference, cm (Female)	102.1±12.8	106.7±12.6 [*]	105.6±15.2	106.1±14.3	109.0±10.3	109.2±9.8	113.4±16.1			
Fasting Glucose, mg/dL	87.5±5.9	101.3±8.7 [*]	99.7±9.5	92.6±10.5 ^{**}	174.6±60.0 [‡]	118.9±16.3	101.8±9.6 ^{‡‡}			
2 hr glucose, mg/dL	101.5±19.9	140.7±31.4 [*]	140.2±31.8	114.5±37.8 ^{**}	234.6±44.0 [‡]	218.6±40.3	146.6±33.5 ^{‡‡}			
HbA _{1c} , %	5.3±0.2	6.0±0.2 [*]	5.6±0.4	5.9±0.2 ^{**}	8.2±1.6 [‡]	6.0±0.4	6.6±0.2 ^{‡‡}			
Insulin, mIU/L	8.8±5.8	14.1±8.2 [*]	11.4±8.1	10.9±6.3	16.1±9.7 [‡]	15.3±8.3	13.6±6.6			
Systolic BP, mmHg	125.6±17.8	131.8±17.0 [*]	132.1±18.3	128.0±16.0 ^{**}	137.9±18.7 [‡]	132.2±16.9	129.5±14.8			
Diastolic BP, mmHg	79.8±9.8	82.4±10.2 [*]	80.5±10.0	80.4±9.0	83.3±10.4 [‡]	80.6±9.2	81.2±7.5			
Total Cholesterol, mg/dL	193.5±33.5	203.6±35.8 [*]	204.5±42.9	202.5±39.4	203.0±38.6 [‡]	202.5±40.9	202.0±47.6			
Total Triglycerides, mg/dL	130.3±67.9	160.8±84.8 [*]	159.1±94.8	153.1±87.0	208.4±102.4 [‡]	172.6±110.3	157.9±84.9			
HDL ⁻ , mg/dL	50.2±14.1	46.8±12.5 [*]	49.1±13.4	47.8±13.5	44.5±11.8 [‡]	51.8±22.8	44.1±11.5 ^{‡‡}			

Characteristics	NORMAL		PREDIABETES				DIABETES			
	A. NG	B. (+)PGC (+)HbA1c	C. (+)PGC (-)HbA1c	D. (-)PGC (+)HbA1c	E. (+)PGC (+)HbA1c	F. (+)PGC (-)HbA1c	G. (-)PGC (+)HbA1c			
LDL ² , mg/dL	117.2± 29.4	124.6±32.0 [*]	123.6±38.2	124.0±33.0	116.7± 34.9	116.2± 31.8	126.3± 37.0			
Hs-CRP, mg/L	4.7± 5.4	6.7±7.4 [*]	5.7±6.2	6.4±6.8	8.2± 5.2 [‡]	8.1± 8.1	9.5± 8.4			
HOMA IR	1.9± 1.3	3.5±2.1 [*]	2.8±2.1	2.5±1.7 ^{**}	6.5± 3.8 [‡]	4.6± 2.8	3.4± 1.7 ^{‡‡}			
Insulinogenic Index	1.6± 4.5	0.9±0.7 [*]	0.9±0.8	1.2±4.8	0.21± 0.21	0.34± 0.70	0.72± 0.62 ^{‡‡}			
Disposition Index	0.95± 2.12	0.30±0.20 [*]	0.38±0.26	0.65±1.99	0.04± 0.04 [‡]	0.07± 0.37	0.22± 0.14 ^{‡‡}			

^{*} A vs. B, p< 0.05;

^{**} C vs. D, p< 0.05;

[‡] A vs E, p< 0.05;

^{‡‡} F vs G, p<0.05;

¹ high density lipoprotein;

² low density lipoprotein

Table 2
Cross tabulation of diabetes and prediabetes diagnoses by using the OGTT vs the HbA_{1c}

		Plasma Glucose Criteria			
		NORMAL	PREDIABETES	DIABETES	TOTAL
HbA _{1c}	NORMAL	403	124	13	540
	PREDIABETES	401	278	38	717
	DIABETES	9	18	58	85
	TOTAL	813	420	109	1,342

Table 3

Association of HbA_{1C} and plasma glucose criteria with insulin resistance (HOMA-IR 4th quartile of normal glucose subjects) and impairment in pancreatic β cell insulin secretory capacity (disposition index and insulinogenic index 1st quartile of normal glucose subjects).

	OR (95% CI)
HOMA: Insulin Resistance	
PGC-Prediabetes	3.3 (2.4, 4.5)
HbA _{1c} -Prediabetes	2.1 (1.5, 2.9)
PGC-Diabetes	17.9 (11.0, 29.3)
HbA _{1c} -Diabetes	12.6 (7.2, 21.8)
Disposition index: β Cell function	
PGC-Prediabetes	7.3 (5.3, 10.1)
HbA _{1c} -Prediabetes	3.2 (2.3, 4.4)
PGC-Diabetes	133.1 (55.5, 319.4)
HbA _{1c} -Diabetes	38.9 (18.5, 81.7)
Insulinogenic index: Impaired Insulin Secretion	
PGC-Prediabetes	2.7 (2.0, 3.6)
HbA _{1c} -Prediabetes	1.0 (0.7–1.3) *
PGC-Diabetes	27.0 (14.6, 50.0)
HbA _{1c} -Diabetes	15.1 (7.7–29.6)

Models adjusted for age, sex, BMI and waist circumference.

* Only non-significant association