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Publication Date

2018

DOI

10.1016/j.diabres.2017.11.010

Peer reviewed

The GLP-1 Response to Glucose Does Not Mediate Beta and Alpha Cell Dysfunction in Hispanics with Abnormal Glucose Metabolism

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Abstract

Aims—Glucagon-like peptide-1 (GLP-1) contributes to insulin secretion after meals. Though Hispanics have increased risk for type 2 diabetes mellitus, it is unknown if impaired GLP-1 secretion contributes to this risk. We therefore studied plasma GLP-1 secretion and action in Hispanic adults.

Methods—Hispanic (H; n=31) and non-Hispanic (nH; n=15) participants underwent an oral glucose tolerance test (OGTT). All participants were categorized by glucose tolerance into four groups: normal glucose tolerant non-Hispanic (NGT-nH; n = 15), normal glucose tolerant Hispanic (NGT-H; n = 12), impaired glucose tolerant Hispanic (IGT-H; n = 11), or newly diagnosed type 2 diabetes mellitus, Hispanic (T2D-H; n = 8).

Results—Glucose-induced increments in plasma GLP-1 (Δ-GLP-1) were not different in NGT-H and NGT-nH (p=0.38), nor amongst Hispanic subgroups with varying degrees of glucose homeostasis (p=0.6). In contrast, the insulinogenic index in T2D-H group was lower than the other groups (p=0.016). Subjects with abnormal glucose homeostasis (AGH), i.e., T2D-H plus IGT-H, had a diminished glucagon suppression index compared to patients with normal glucose homeostasis (NGT-H plus NGT-nH) (p=0.035).

Conclusions: GLP-1 responses to glucose were similar in Hispanic and Non-Hispanic NGT—Despite similar glucose-induced -GLP-1, insulin and glucagon responses were abnormal in T2D-H and AGH, respectively. Thus, impaired GLP-1 secretion is unlikely to play a role in islet dysfunction in T2D. Although GLP-1 therapeutics enhance insulin secretion and glucagon suppression, it is likely due to pharmacological amplification of the GLP-1 pathways rather than treatment of hormonal deficiency.

1. INTRODUCTION

Type 2 Diabetes Mellitus (T2D) has become a major public health concern in the United States. As of 2014, diabetes affected 29.1 million people or 9.3% of the U.S. population[1]. The risk of diagnosed diabetes is 66% higher among Hispanics in comparison to non-Hispanic white adults[2]. Insulin secretory dysfunction is an important contributor to T2D, and pathways responsible for endogenous insulin secretion are opportunities for pharmacological intervention. In healthy subjects, a large part of the postprandial insulin response is due to the actions of the incretin hormones, glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)[3]. However, in T2D the incretin effect is impaired, resulting in the inability to efficiently dispose of glucose[3]. While the two incretin hormones, GLP-1 and GIP, are responsible for about 50–70% of the postprandial insulin responses in healthy individuals, it has been estimated that they contribute only about 20% of the insulin response after oral glucose ingestion in T2D[4].

Although Hispanics have an increased risk of T2D, it is not known if GLP-1 secretion contributes to this risk. There has been limited research into ethnic and racial differences in GLP-1 secretion. A study of obese, but otherwise healthy African Americans demonstrated higher GLP-1 concentrations during fasting and an oral glucose tolerance test (OGTT) when compared with a Caucasian group[5]. Another study amongst Japanese T2D, not compared with any other ethnic group, showed no significant differences in GIP or GLP-1 during an OGTT or meal tolerance test in various stages of glucose intolerance[6].

To our knowledge, no studies have looked specifically at GLP-1 physiology or pathophysiology in the Hispanic-American population, or compared this group to other ethnic groups.

2. METHODS

2.1. Participants

Self-declared Hispanic participants (n=31) in this study were part of a previously described family-based study in which participants had a family history of T2D and were of Mexican or Central American heritage[7]. Non-Hispanic Caucasian subjects (n=15) were recruited simultaneously, to include non-obese participants without a family history of diabetes. All subjects were healthy, with no known history of gastrointestinal diseases associated with

malabsorption, autoimmune diseases, acute or chronic infections, malignant diseases, renal disease, liver disease or any conditions known to impair glucose tolerance. Subjects provided written informed consent, and the study was approved by the IRB of the Los Angeles Biomedical Research Institute.

2.2. Procedures

Participants were asked to fast for 8–10 hours before baseline blood samples were collected for an OGTT. Participants ingested a 75-gram glucose solution, and blood samples were collected before and at 10–60 min intervals over the ensuing four hours[8]. Dietary information for each participant was collected and analyzed to ensure that at least 200 grams of carbohydrate per day for three days had been ingested prior to the study[8,9].

2.3. Analyses

Data collected on the day of the OGTT included measurements of weight, height, waist circumference, percent fat measured by bioelectrical impedance analysis (BIA), diastolic and systolic blood pressure, and blood and urine samples for measurement of serum lipids (high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol, triglycerides), glycated hemoglobin (HbA$_1$C), liver enzymes (alanine transaminase (ALT) and aspartate transaminase (AST)), estimated glomerular filtration rate (eGFR) and urinary albumin to creatinine ration (UACR). The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) Study equation[7].

Plasma glucose, insulin, and glucagon, were collected at all time points during the OGTT. Samples for GLP-1 were collected at 1 min prior to (−1) and at 30 min after glucose ingestion. Glucose and insulin measurements from the -1 and 30 min samples were used to estimate the **insulinogenic index**, which was defined as (Insulin)/(Glucose) for the respective increments ( ) in insulin and glucose between −1 and 30 min.[10]. A glucagon suppression index (GSI) was also derived to evaluate the effect of glucose to suppress plasma glucagon concentrations. This index was estimated using all available samples from the OGTT. The GSI was defined using glucose and glucagon samples, as (Glucagon)*(−1)/ Glucose, where the lowest recorded glucagon concentration was used to calculate the decrement in glucagon compared with baseline, and the highest preceding glucose concentration was used to derive the increment in glucose compared with each respective baseline, at −1 min. Homeostasis Model Assessment (HOMA-IR) was estimated using the equation: HOMA-IR = (I*G)/22.5, where I=fasting insulin (uU/mL) and G=fasting glucose (mmol/L)[7].

Measurements to assess body composition and fat free body mass included height and weight to calculate body mass index (BMI) and BIA[11,12]. Waist circumference was measured by palpating the top of the iliac crest and then placing the measuring tape around the trunk at this level[13,14].

Samples for GLP-1 were collected in tubes that contained a DPP-4 inhibitor, and were analyzed using a total GLP-1 ELISA (7–36 and 9–36) kit from ALPCO®[15]. Samples for GLP-1 were unavailable for 4 subjects. Plasma glucose was measured using standard

laboratory procedures and plasma insulin and glucagon were measured by radioimmunoassay as previously described[16]. Samples for glucose were measured in two different laboratories. To provide within-subject consistency, glucose measurements for each individual participant used for analysis were measured in the same lab. The range of detection for the glucose, insulin and glucagon assays was 0–29.4 mmol/L, 9–69,450 pmol/L and 2.9–114.8 pmol/L, respectively. Glucagon measurements were available for only 27 subjects.

2.4. Data analysis

Participants were grouped according to ethnicity, Hispanic (H) versus non-Hispanic (nH) and according to degree of glucose tolerance based upon standard criteria of the American Diabetes Association. Groups were defined as normal glucose tolerant (NGT), impaired glucose tolerant (IGT), or type 2 diabetes mellitus (T2D)[17]. All patients with T2D were newly diagnosed at the time of or just prior to the OGTT, and all were medication naive. Insulinogenic index as well as GLP-1 increments were only calculated for participants with available GLP-1 data (n=42). Due to the smaller number of participants with glucagon data (n=27), we combined the two NGT groups (Hispanic and non-Hispanic) into a single normal glucose homeostasis (NGH) group (n=17). The IGT and T2D groups were also combined into a corresponding abnormal glucose homeostasis (AGH) group (n=10). Data were analyzed using Number Crunching Statistical System (NCSS) (2007 version, Kaysville, UT). Data are presented as median and interquartile range [IQR], and analyzed using either the Kruskal-Wallis or Mann-Whitney tests, as appropriate for multiple or two-group testing by ranks. Chi-Square test was used for categorical data. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Characteristics of participants

A convenience sample of 46 participants was used in this study. As summarized in Table 1, the participants were primarily female (n=30; 65%) and Hispanic (n=31; 67%), with a median age of 41 years [25–52]. There were eight participants with newly diagnosed with T2D, 11 with IGT, and 27 with NGT (Hispanic, n= 12; non-Hispanic, n=15). None of the patients with T2D was receiving diabetes medications at the time of the study. Median BMI for the study population was 27.3 Kg/m^2 [23.1–30.7].

3.2. Comparison of Hispanic and Non-Hispanic participants with normal glucose tolerance

As illustrated in Table 2, the two NGT groups were similar in a number of respects (BMI, waist circumference, blood pressure, serum triglyceride, HbA1c, liver enzymes, eGFR, UACR and HOMA-IR), though the NGT-nH group was younger than the NGT Hispanic group (p=0.013). When the NGT-nH and NGT-H groups were compared for other baseline characteristics, the only other significant difference besides age was the percent body fat (p=0.03). There were no significant differences in BMI, waist circumference, systolic or diastolic blood pressure or lipid parameters (serum LDL, HDL, triglyceride) (Table 2).

3.3. Comparison of all study groups

When the NGT-nH group was compared with all Hispanic groups, NGT-H was also younger than the Hispanic groups (median age 26 y) compared to the Hispanic groups (median age of 39, 50, and 50.5y, for the NGT-H, IGT-H, and T2D-H groups respectively). BMI, waist circumference, percent body fat, systolic blood pressure, low-density and total cholesterol, triglyceride, HbA1C and HOMA-IR were significantly different amongst the four groups; higher in the IGT and T2D groups, as expected (Table 2).

3.4. GLP-1 increment during the OGTT

The increment in GLP-1 (Δ-GLP-1) concentrations after glucose ingestion was not different in the NGT groups, when Hispanic and non-Hispanic with normal glucose tolerance were compared (Table 3; p=0.38). There was also no difference in the median increase in GLP-1 between the groups of varying glucose homeostasis (Table 3). When compared between the four groups, ΔGLP-1 was not significantly different (p=0.56, by ANOVA). To determine if Δ-GLP-1 was different in the T2D group alone, this group was compared with the other three non-diabetic groups combined. Median Δ-GLP-1 in T2D (n=8) was 3.9 pmol/L [3.08–6.36], and was slightly, but not significantly higher than the other three groups combined (n=34), 3.0 pmol/L [1.93–5.03] (p=0.28). The T2D group had the highest median Δ-GLP-1 concentration, which illustrates that newly diagnosed, untreated T2D does not diminish the Δ-GLP-1 response to glucose.

3.5. Insulinogenic index, and glucagon suppression index during OGTT

In contrast to the Δ-GLP-1 results, the insulinogenic index was not the same when all four groups were compared (p=0.016). The results are summarized in Table 3. When the T2D group alone was compared with the other three groups combined, there was a statistically significant lower median insulinogenic index, 0.42 pmol/L vs 0.996 pmol/L (p=0.003). Thus, despite a Δ-GLP-1 after glucose stimulation in T2D that was at least as large as the other groups, the insulinogenic index was significantly suppressed in those with T2D.

The glucagon suppression index was evaluated in all participants with available data. Those with abnormal glucose homeostasis (T2D-H + IGT-H, n=10) were found to have a significantly lower glucagon suppression index (Median = 0.25 [0.2–0.55]) compared to patients with normal glucose homeostasis (NGT-nH + NGT-H, n=17) (Median = 0.53 [0.39–0.88]), p = 0.035, as summarized in Table 4. Thus, glucose was more effective in suppressing glucagon secretion in participants with NGH than those with AGH, a classic and well-known observation[18]. These results also illustrate that despite an adequate GLP-1 increment in response to glucose, the glucagon decrement in response to glucose is significantly impaired in participants with abnormal glucose homeostasis.

4. DISCUSSION

This study has demonstrated that GLP-1 physiology in Hispanics and Non-Hispanics appears not to differ in response to glucose ingestion. The Δ-GLP-1 response was similar during an OGTT in Hispanics and Non-Hispanics who have normal glucose tolerance. Considering that the Hispanics in this study had a family history of T2D, and the non-

Hispanics did not, this also suggests that neither ethnicity nor family history of diabetes influence the GLP-1 response to glucose, at least when comparing these two ethnic groups.

We also examined whether different degrees of glucose homeostasis influenced the GLP-1 response to oral glucose. No difference was evident in the -GLP-1 response to glucose when participants with NGT were compared with those who have abnormal glucose homeostasis, whether IGT, T2D were evaluated separately or combined. GLP-1 responses thus do not seem to be affected by Hispanic ethnicity in persons with normal glucose tolerance, nor by degree of glucose intolerance within this ethnic group.

Previous studies of non-Hispanics have not been definitive on whether GLP-1 secretion is affected in states of abnormal glucose homeostasis. Some investigators have shown impairment in GLP-1 secretion after ingestion of a meal or glucose in patients with T2D[19–23]. In contrast, other studies have found no reduction in GLP-1 levels in patients with T2D[6,24–27].

Although it is well-recognized that Hispanics have an increased risk of developing T2D, it is not known if GLP-1 secretion contributes to this risk. The results of this study suggest GLP-1 secretion does not play that role. Despite similar GLP-1 responses to glucose in all groups, the expected abnormalities in insulin and glucagon secretion that occur in states of abnormal glucose homeostasis were observed in this study. The insulinogenic index, an estimate of glucose-induced insulin secretion, was impaired in Hispanics with T2D. Similarly, the glucagon suppression index was abnormal in the altered glucose homeostasis group, evidence for impaired suppression of alpha cell function. This suggests that in Hispanics with T2D or abnormal glucose homeostasis, insulin and glucagon responses to glucose are abnormal despite adequate secretion of GLP-1. Therefore, impaired GLP-1 secretion is unlikely to play a role in islet dysfunction in T2D.

Velasquez-Mieyer studied GLP-1 in obese, but otherwise healthy African Americans during an oral glucose tolerance test (OGTT)[5]. They found that at comparable levels of insulin resistance, glucose tolerance, BMI, waist-to-hip ratio, waist circumference, leptin, and fat mass, African Americans had higher concentrations of GLP-1 both when fasting and during an OGTT, compared to a Caucasian group[5]. That study suggested that higher baseline and stimulated GLP-1 levels amongst African Americans might explain the higher insulin response and prevalence of hyperinsulinemia commonly seen in the African American population.

A study of GLP-1 secretion in Japanese T2D supports our findings[6]. Despite an impaired early phase insulin secretion and reduced glucagon suppression, no significant differences were found in GIP or GLP-1 during an OGTT or meal tolerance test amongst groups with NGT, IGT or T2D[6].

It has been recently shown that Insulin-like growth factor-1 (IGF-1) may play a regulatory role in glucagon secretion in Caucasian subjects without diabetes[28]. The impaired glucagon suppression index seen in our abnormal glucose tolerance group thus could be mediated by an effect of altered IGF-1 concentrations in the alpha cells. However, IGF-1 was not

measured in our study so we do not have data to address this question in Hispanics with T2D.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) are efficacious in Hispanic patients with type 2 diabetes. A recent review of six GLP-1 RA found that use of either long duration or short acting GLP-1 RA resulted in consistent reductions in HbA1c and weight, as well as consistently low rates of hypoglycemia. Six of the 10 trials reviewed included Hispanic or Latin American participants (11–33% of total study subjects)[29]. This effectiveness of drugs to improve glycemic control suggests that in Hispanics, as in other population groups, the GLP-1 pathway in the beta cell is functional and responsive to pharmacological stimulation.

This study had several limitations. Sample size is relatively small, but is unlikely to contribute to the apparent lack of a significant difference in the GLP-1 responses to glucose ingestion in the different groups. This is because there was little variation in the median responses in the four groups, indeed the median -GLP-1 in T2D was non-significantly higher than the other groups, even when all three non-diabetic groups were combined. The data in this study are supported by others in which GLP-1 response to glucose was unaffected by abnormalities in glucose homeostasis[6, 24–26]. Another concern for studies such as this is the specificity and sensitivity of commercially available assays for glucagon measurement as recently reported[30]. Of the RIA assay kits tested in that report, the RIA kit used in our study (Millipore) performed best with a sensitivity around 10 pmol/L. Three assays, including the Millipore assay, were found to be specific for glucagon but exhibited a small cross-reactivity with oxyntomodulin and glicentin[30]. Lastly, the analytical method for GLP-1 measurement used in this study was not able to differentiate between active GLP-1 and total GLP-1. Differences in GLP-1 detection methods have been suggested as a potential factor in the discrepant findings in studies of stimulated GLP-1 secretion in patients with type 2 diabetes[26,27]. It is difficult to gauge the impact of the GLP-1 analytical method we used (total GLP-1) on our results as Lee et al. showed similar findings, with no significant differences in GLP-1 during an OGTT or meal tolerance test in various stages of glucose intolerance, while measuring active GLP-1[6]; total GLP-1 has recently been shown to positively correlate with active GLP-1 concentration[31]; and some researchers have suggested that total GLP-1 levels are better indicators of the overall GLP-1 secretory response because intact GLP-1 assays are often compromised by readings below the lower limit of detection and by large variations in peripheral measurements[27]. Nevertheless, care should be taken when comparing results from studies that use assays that employ different targets (active or total GLP-1) or different methods.

In conclusion, to our knowledge this study is the first to investigate GLP-1 secretion and action in the Hispanic-American population. Our results suggest that it is unlikely that abnormalities in GLP-1 secretion contribute to the pathogenesis of T2D amongst Hispanics. Our findings further suggest that although GLP-1 therapeutic agents enhance insulin secretion and glucagon suppression in patients with type 2 diabetes, these effects likely result from pharmacological amplification of GLP-1 pathways rather than the treatment of a hormone deficiency.

Acknowledgments

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Highlights

- In Type 2 diabetes (T2D) insulin secretion and glucagon suppression is impaired

- We tested if an impaired GLP-1 pathway can account for T2D in Hispanic Americans

- Glucose stimulated GLP-1 secretion is similar in non-Hispanic, Hispanic and T2D

- In T2D impaired insulin and glucagon responses were found despite normal GLP-1

- GLP-1 therapies do not rely on replacement, rather amplification of GLP-1 pathways

TABLE 1

Characteristics of Study Participants

Variables	Summary
n	46
Gender (M/F)	16/30
Ethnic category (H/nH)	31/15
Age (years)	41 [25 – 52]
Weight (kg)	74.4 [64.5 – 85.5]
BMI (kg/m^2)	27.3 [23.1 – 30.7]
Waist-C (cm)	94.4 [87.3 – 102.9]
% Fat - BIA	34.4 [26.9 – 40.9]

Abbreviations: M, male; F, female; H, Hispanic; nH, Non-Hispanic; BMI, body mass index; Waist-C; waist circumference; % Fat - BIA, percent fat measured by bioelectrical impedance analysis

Data expressed as median and interquartile range [IQR]

TABLE 2

Demographic Characteristics of Study Participants According to Study Group

	NGT-nH	NGT-H	IGT-H	T2D-H
n	15	12	11	8
Gender (M/F)	8/7	2/10	3/8	3/5
Age (years)[ac]	24 [22.5 – 26]	39 [26 – 48]	50 [42.5 – 54]	50.5 [47.5 – 56]
Weight (kg)[a]	78.6 [64.3 – 85.2]	64.6 [60.7 – 74.6]	77.7 [71.3 – 92.4]	85.6 [71.2 – 92.9]
BMI (kg/m^2)[a]	23 [22.5 – 25.2]	25.7 [23.1 – 29.1]	30.9 [28.2 – 34]	30.7 [29.2 – 32.3]
Waist-C (cm)[a]	89.6 [84.6 – 92.9]	94.8 [85.6 – 96.7]	103.3 [97.2 – 112.5]	104.3 [99.5 – 111.9]
%Fat-BIA[bc]	26.6 [25.3 – 29.2]	35.6 [28.2 – 41.3]	36.3 [31.2 – 44.6]	39.5 [35.6 – 41.3]
Blood Pressure - Systolic (mmHg)[a]	123 [114 – 125.5]	111 [107.3 – 118.5]	138 [120 – 147.5]	137 [124 – 144.5]
Blood Pressure -Diastolic (mmHg)	66 [63 – 70.5]	66.5 [61.8 – 70.3]	77 [63 – 83.5]	72.5 [66.5 – 77.3]
Laboratory Data:				
HDL (mmol/L)	1.0 [1.0 – 1.3]	1.1 [1.1 – 1.4]	1.1 [1.0 – 1.3]	1.2 [0.9 – 1.3]
LDL (mmol/L)[b]	2.3 [2.2 – 3.0]	3.0 [2.5 – 3.8]	3.8 [3.3 – 4.3]	2.8 [2.6 – 3.4]
Chol (mmol/L)[b]	3.9 [3.7 – 4.6]	4.6 [4.2 – 5.4]	5.9 [5.6 – 6.6]	4.9 [4.5 – 5.4]
TG (mmol/L)[a]	0.9 [0.6 – 1.0]	1.0 [0.6 – 1.2]	1.7 [1.2 – 2.3]	1.7 [1.6 – 2.3]
HbA1c (%) (mmol/mol)[ac]	5.4 [5.0 – 5.5] (36 [31 – 37])	5.4 [5.2 – 5.7] (36 [33 – 39])	5.6 [5.4 – 6.0] (38 [36 – 42])	6.5 [6.3 – 6.8] (48 [45 – 51])
ALT (U/L)	23 [17 – 25.5]	22.5 [16.8 – 28]	24 [21 – 29]	26 [22.5 – 38.5]
AST (U/L)	22 [17.5 – 25.5]	25 [18.8 – 29]	27 [24.5 – 30.5]	27 [25.5 – 33.5]
eGFR (mL/min/1.73m^2)	89.8 [79.8–96.8]	106.6 [95.5–115]	110.8 [104.9–116.4]	91.4 [86.9–107.5]
UACR (mg/mmol)	0.3 [0.2 – 0.5]	0.6 [0.5 – 0.6]	0.5 [0.4 – 1.1]	0.8 [0.6 – 1.9]
HOMA-IR (units)[b]	1.0 [0.6 – 1.1]	1.0 [0.7 – 1.2]	2.0 [1.2 – 3.3]	3.6 [2.4 – 5.4]

Abbreviations: NGT-nH, Normal Glucose Tolerance, non-Hispanic; NGT-H, Normal Glucose Tolerance, Hispanic; IGT-H, Impaired Glucose Tolerance, Hispanic; T2D-H, Type 2 Diabetes, Hispanic; M, male; F, female; BMI, body mass index; Waist-C, waist circumference; % Fat-BIA, percent fat measured by bioelectrical impedance analysis; HDL, high density lipoprotein; LDL, low density lipoprotein; Chol, cholesterol; TG, triglycerides; HbA1c, hemoglobin A1c; ALT, alanine transaminase; AST aspartate transaminase; eGFR, estimated glomerular filtration rate; UACR, urinary albumin to creatinine ratio; HOMA-IR, homeostatic model assessment-insulin resistance Data expressed as median and interquartile range [IQR]

[a] $p<0.001$,

[b] <0.01, comparing all groups

[c] <0.05, comparing NGT-H with NGT-nH

TABLE 3

GLP-1Data and Insulinogenic Index for Study Participants According to Study Group

	NGT-nH	NGT-H	IGT-H	T2D-H
n	15	12	11	8
GLP-1				
GLP-1_-1 minute (pmol/L)	1.4 [0.9 – 2.6]	1.0 [0.8 – 1.3]	1.3 [1 – 3]	0.9 [0.7 – 1.4]
GLP-1 30 minutes (pmol/L)	4.8 [2.7 – 12.3]	4.4 [2.4 – 5.4]	5.9 [4.4 – 10.4]	5.1 [4.2 – 7.5]
Median GLP-1 (pmol/L) [*]	3.0 [2.3 – 7.6]	3.0 [1.2 – 3.4]	3.5 [2.6 – 6.3]	3.9 [3.1 – 6.4]
Median Insulinogenic Index [**]	0.8 [0.6 – 1.3]	1.1 [0.9 – 1.7]	1.0 [0.8 – 1.2]	0.4 [0.3 – 0.6]

[*] *P* = 0.56. *By* Kruskal-Wallis One-way ANOVA test

[**] *P* = 0.016. *By* Kruskal-Wallis One-way ANOVA test

Abbreviations: (See Table 2); GLP-1, glucagon like peptide – 1

Data expressed as median and interquartile range [IQR]

TABLE 4

Effect of Glucose Ingestion on Glucagon Suppression Index

	n	Median GSI
Abnormal Glucose Homeostasis	10	0.3 [0.2 – 0.6]
Normal Glucose Homeostasis	17	0.5 [0.4 – 0.9]

$P = 0.035$. P value was obtained using a Mann-Whitney U test

Abbreviations: (See Table 2); GSI, glucagon suppression index

Data expressed as median and interquartile range [IQR]