RACIAL DISPARITY IN GLUCAGON-LIKE PEPTIDE 1 (GLP-1) AND INFLAMMATION MARKERS AMONG SEVERELY OBESE ADOLESCENTS

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Running title: Racial disparity in GLP-1

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ABSTRACT

Objective: Compared with Caucasians (C), obese African-American (AA) adolescents have higher risk for type 2 diabetes. Subclinical inflammation and reduced GLP-1 concentration are linked to the pathogenesis of the disease. We determined the relationship between insulin resistance, β-cell activity, and sub-clinical inflammation with GLP-1 concentrations, and whether racial disparities in GLP-1 response were present in 49 obese adolescents (14 ± 3 y, 76% AA, 71% female).

Research Design And Methods: Subjects underwent physical examination and an oral glucose tolerance test. We measured levels of high sensitivity CRP (CRP$_{hs}$), fibrinogen, glucose, GLP-1$_{total}$, GLP-1$_{active}$, and insulin. Insulin and glucose area under the curve, insulinogenic index ($\Delta$I30/$\Delta$G30), and composite insulin sensitivity index (CISI) were computed. Subjects were categorized by race and as inflammation-positive (INF+) if CRP$_{hs}$ or fibrinogen were elevated.

Results: No racial differences were seen in mean or relative BMI. Thirty-five percent of subjects had altered fasting or 2-hour glucose levels (AA vs. C, $P = NS$), and 75% were INF+ (AA vs C, $P = 0.046$). Glucose and insulin, CISI, and $\Delta$I30/$\Delta$G30 values were similar; AA had lower GLP-1$_{total}$AUC ($P = 0.01$), GLP-1$_{active}$ at 15 min ($P = 0.03$), GLP-1$_{active}$AUC ($P = 0.06$), and higher fibrinogen ($P = 0.01$) and CRP$_{hs}$ ($P = NS$) compared with C.

Conclusion: AAs exhibited lower GLP-1 concentrations and increased inflammatory response. Both mechanisms may act synergistically to enhance obese AA predisposition to type 2 diabetes. Our findings might be relevant to effective deployment of emerging GLP-1-based treatments across ethnicities.
Childhood obesity has reached epidemic proportions in the United States. Obesity prevalence and rate of increase among African-American (AA) adolescents are twice as great as those among Caucasian (C) adolescents. Type 2 diabetes mellitus in children also has increased alarmingly and emerged as a critical health issue (1). Consequently, AA adolescents have the highest incidence and prevalence of type 2 diabetes (2). Disparities in insulin dynamics, glucose production or some combination of factors have been suggested to explain the increased risk for AA to develop type 2 diabetes (3; 4). However, little is known about whether an interaction of the inflammatory response and insulin resistance could affect glucagon-like peptide-1 (GLP-1) responses (incretin responses) and contribute to the increased risk for type 2 diabetes in obese AA adolescents.

Elevated levels of high-sensitivity C-reactive protein (CRP$_{hs}$) have been associated with increased risk for type 2 diabetes and cardiovascular disease (CVD) (5). Previous studies in children and adults have shown that there are racial differences in inflammatory markers (6). AA individuals exhibited higher levels of CRP$_{hs}$ and fibrinogen (Fib) at comparable levels of obesity and fitness. The role of GLP-1 as a major regulator of glucose homeostasis has been demonstrated (7). We have previously shown racial differences in enteroinsular axis activity in obese adults. As compared with C, AA subjects exhibited higher basal and glucose-stimulated concentrations of total GLP-1 (GLP-1$_{total}$, mostly inactive), which persisted after six months of treatment with a long-acting somatostatin analog (8), suggesting that racial disparities could be present in the mechanisms that regulate the secretion, degradation or clearance of GLP-1. In a biracial sample of obese adolescents we sought to evaluate how indices of insulin resistance, β-cell activity and sub-clinical inflammation relate to active (GLP-1$_{active}$) and total (GLP-1$_{total}$) GLP-1 concentrations, and whether racial disparities in GLP-1 response are present in obese adolescents.

**RESEARCH DESIGN AND METHODS**

All subjects gave written informed consent prior to eligibility confirmation. Forty-nine adolescents between the ages of 11 and 18 y, with a body mass index (BMI) $\geq$ 85th percentile for age and gender and not taking any medication, were recruited for this study. For the oral glucose tolerance test (OGTT), each subject consumed 1.0 g dextrose/kg of body weight (Allegiance, MacGaw Park, IL) up to a maximum of 75 g, and blood samples were obtained at 0, 15, 30, 60, 90, and 120 minutes (9). The following indices from the OGTT were computed: areas under the curve (10) for insulin (IAUC), glucose (GAUC), total GLP-1 (GLP-1$_{total}$ AUC) and active GLP-1 (GLP-1$_{active}$ AUC). We chose AUC to estimate as a single value both magnitude and duration of the response for insulin, glucose, GLP-1$_{active}$ and GLP-1$_{total}$ to glucose load over time, and only absolute concentrations were used to report fasting insulin, glucose and GLP-1 at baseline and at 15 minutes. Insulinogenic index ($\Delta$I$_{30}$/\DeltaG$_{30}$) and composite insulin sensitivity index (CISI) = 10000/ square root [(fasting insulin x fasting blood glucose) x (mean insulin (0 - 120 min) x mean glucose (0 - 120 min)] were used as surrogate markers of β-cell function and insulin sensitivity, respectively (1). A subject’s glucose tolerance status was defined based on the 2007 American Diabetes Association criteria (11). Subjects were classified as either having normal glucose tolerance (NGT = fasting plasma glucose concentration < 100 mg/dl and plasma post-load glucose level < 140 mg/dl), or impaired glucose metabolism (IGM). IGM included impaired fasting glucose (IFG = fasting
glucose level of 100-125 mg/dl), impaired glucose tolerance (IGT = a two-hour plasma glucose level ≥ 140 and < 200 mg/dl), or diabetes (fasting glucose concentration > 126 mg/dl or a two-hour post-load glucose level of ≥ 200 mg/dl).

Serum glucose was measured by the glucose oxidase method (12). Serum immunoreactive insulin (μU/ml) from each OGTT sample was measured by standard double-antibody radioimmunoassay (RIA) (Linco Research, St Louis, MO). Samples for GLP-1 were collected into iced vacutainer tubes (Becton Dickinson, UK) prepared with EDTA and DPP-IV inhibitor (Linco Research) for preventing active GLP-1 [GLP-1 \(_{7-37}\), GLP-1 \(_{7-36}\)] degradation into truncated, inactive GLP-1 [GLP-1 \(_{9-37}\); GLP-1 \(_{9-36}\)]. GLP-1 total was determined using a specific C-terminal antibody RIA that binds to the C-terminal portion of GLP-1, both amidated and non-amidated forms (GLP1T-36HK, Linco Research). GLP-1 active (GLP-1 \(_{7-37}\), GLP-1 \(_{7-36}\),) was measured by ELISA using a specific N-terminal region monoclonal antibody (EGLP-35K, Linco Research).

CRP \(_{hs}\) levels were determined using latex immunonephelometry at the University of Miami Diabetes Institute. Fibrinogen levels were measured using modified thrombin time with photo-optical measurement of turbidity (13). CRP \(_{hs}\) levels were considered elevated if values were ≥ 2 mg/l, and fibrinogen was considered increased if values were ≥ 350 mg/dl. The sample was stratified as sub-clinical inflammation-positive (Inf +) if either CRP \(_{hs}\) or fibrinogen or both were elevated, and as sub-clinical inflammation negative (Inf-) if neither were elevated.

Statistical data analyses were performed using the SAS system (Cary, NC). Descriptive statistics are reported as means and standard error of the mean (SEM) for continuous data and frequencies and percentage for categorical data. Area under the curve (AUC) was calculated by the trapezoidal method (10). Subjects were stratified and analyzed by race, glucose tolerance status, and inflammatory markers. Statistical analyses consisted of \(\chi^2\), Fisher's exact test, Pearson correlation estimation, analysis of variance and analysis of covariance (RBMI adjustment was done for CISI, \(\Delta I30/\Delta G30\), fibrinogen and CRP \(_{hs}\)). For continuous variables adjusted for RBMI, least-squares means ± SEM are reported. \(P\) values ≤ 0.05 were considered significant and a trend toward significance was defined by a \(P > 0.05\) and ≤ 0.10.

**RESULTS**

Forty-nine subjects (71.4 % female, 76% AA) were included in the analysis. For the total sample, age was 14.1 ± 1.9 y; weight, 98.0 ± 22.7 kg; BMI, 36.0 ± 7.5 kg/m\(^2\); and RBMI, 183.7 ± 35.4. Seventeen subjects (35%) had IGM, 28 (57%) had blood pressure higher than the 95th percentile, and 75% of the subjects were Inf+. None of the clinical characteristics was statistically different between racial groups, except for AAs having a trend toward higher prevalence of Inf+ (\(\chi^2 = 5.3\), \(P = 0.046\)) and increased blood pressure (\(\chi^2 = 4.7\), \(P = 0.09\)) (Table 1).

Mean values for indicators of insulin dynamics, inflammatory markers and the enteroinsular axis (EIA) for the entire sample, stratified by race, are presented in Table 2. Racial groups exhibited similar values for CISI, \(\Delta I30/\Delta G30\), fasting glucose and insulin, IAUC, and GAUC. AA adolescents exhibited higher fibrinogen levels (\(P = 0.03\)) and a lower GLP-1 response as compared to C, as suggested by lower GLP-1 total-AUC (\(P = 0.01\)), GLP-1 active AUC (\(P = 0.06\)), and GLP-1 active at 15 minute (\(P = 0.03\)). Although fasting values for GLP-1 total and GLP-1 active were also lower among AA adolescents, these differences were not statistically significant (Table 2, Figure 1). Both IGM and NGT groups had similar BMI, RBMI, age,
ΔI30/ΔG30, insulin levels, CISI, CRP\textsubscript{hs}, fibrinogen, fasting or stimulated GLP-1\textsubscript{active}. Only fasting glucose (IGM 103 ± 3.7 vs. NGT 89.3 ± 1.8, \(P = 0.002\)) and GLP-1\textsubscript{total}-AUC (IGM 2233 ± 278 vs. NGT 1529 ± 159, \(P = 0.03\)) were significantly different. Subjects with a higher grade of inflammation (Inf\textsuperscript{+}) exhibited higher BMI (37.6 ± 1.2 vs. 31.1 ± 1.7, \(P = 0.008\)) and RBMI (191.1 ± 5.9 vs. 160.0 ± 7.4, \(P = 0.007\)), and lower GLP-1\textsubscript{active}-AUC (\(P = 0.046\)), fasting-GLP-1\textsubscript{active} (1.98 ± 1.86 vs. 10.3 ± 2.4, \(P = 0.004\)) and a trend toward lower 15 min-GLP-1\textsubscript{active} (4.2 ± 1.3 vs. 8.7 ± 2.4, \(P = 0.10\)). The difference in GLP-1\textsubscript{total} concentrations did not reach statistical significance.

Severity of overweight (BMI and RBMI) was equally associated with CISI (\(r = -0.36, P = 0.02\) for both measures), fibrinogen (\(r = +0.47, P = 0.001\) and \(r = +0.45, P = 0.0007\)), and CRP\textsubscript{hs} (\(r = +0.50, P = 0.0003\) and \(r = +0.45, P = 0.0004\)). Indices of the EIA, including fasting GLP-1\textsubscript{active}, were associated with fibrinogen (\(r = -0.31, P = 0.03\)), and GLP-1\textsubscript{total} AUC correlated with glucose AUC (\(r = +0.39, P = 0.02\)). There was a trend toward an association between fasting-GLP-1\textsubscript{active} and CISI (\(r = +0.29, P = 0.07\)), and between GLP-1\textsubscript{active} AUC and both fibrinogen and CISI (\(r = -0.28, P = 0.07\) and \(r = +0.31, P = 0.06\)).

CONCLUSIONS

Relationships among race, severity of obesity, insulin dynamics, and inflammation. Consistent with previous observations (14; 15) this study demonstrates that independently of race, adolescents with obesity exhibit an increased risk for insulin resistance, IGM and sub-clinical inflammation. Indices of β-cell activity and insulin action were equally affected and the prevalence of IGM was similar in both racial groups. For all subjects, severity of overweight appeared to be a major determinant in the development of the above conditions, as suggested by the inverse association between BMI and RBMI with insulin sensitivity and positive correlations with inflammation markers (fibrinogen and CRP\textsubscript{hs}). There is accumulating evidence supporting adiposity, insulin resistance and inflammation as major risk factors associated with an increased risk for type 2 diabetes and CVD (16).

Our results agree with previous findings (5; 15) and underscore the pathophysiological role of adiposity in regulating inflammation and insulin resistance (17) in adolescents (17-19). There are well-documented ethnic disparities in insulin concentrations and actions between AAs and Cs (20; 21), which were less evident in our study population. There is a progressive deterioration of insulin sensitivity as severity of overweight progresses, but once children reach a certain overweight threshold (RBMI > 150\%), insulin sensitivity reaches a maximum deterioration of 55-70\% (22). The mean RBMI in our subjects was 183.7 ± 35.4; they likely had already experienced a maximal reduction in insulin sensitivity, given a mean CISI of 1.68 ± 0.1.

Insulin resistance/hyperinsulinemia could have an independent association with inflammatory marker levels (15). However, in adolescents and young adults, insulin resistance, as assessed by the homeostasis model assessment of insulin resistance, contributed minimally to the variance in sub-clinical inflammation. In agreement with these results, we found no association between CISI and markers of inflammation.

Racial disparities in inflammation markers. Inflammation has been shown to be a pathophysiological path common to several disorders, such as type 2 diabetes, hypertension, and CVD, each of which are known to contribute disproportionately to the burden of mortality and morbidity in AAs (15; 23). In this study, AA adolescents exhibited higher concentrations and
prevalence of inflammatory markers (Tables 1, 2).

It has been suggested that genetic factors are likely to play a role in the inflammatory response in AAs (24; 25). Genes encoding critical pro-inflammatory cytokines, such as interleukins 1 and 6 (IL-1, IL-6) and tumor necrosis factor- α (TNF-α) have important roles in inflammatory diseases (24). Also, AA women are more likely to carry allelic variants known to up-regulate proinflammatory cytokines. Odds ratios for AAs versus Cs in genotypes up-regulating proinflammatory interleukins ranged from 2.1 to 4.9. The proinflammatory cytokine IL6-174 G/G genotype variant was 36.5 times more common among AAs. Genotypes known to down-regulate the anti-inflammatory interleukin 10 were elevated 3.5- and 2.8-fold in AAs. Cytokine genotypes found to be more common in AA women were consistently those that up-regulate inflammation (24).

**Racial disparities in GLP-1 response during OGTT.** A novel finding was that at comparable levels of adiposity, glucose and insulin secretion and sensitivity, AA adolescents exhibited reduced concentrations of GLP-1\textsubscript{total} and GLP-1\textsubscript{active} during OGTT as compared to C adolescents (Table 2), suggesting that racial discrepancies in the mechanisms regulating the production or secretion of GLP-1 could already be present in obese adolescents. The role of GLP-1 (GLP-1\textsubscript{7-37}, GLP-1\textsubscript{7-36}) as a major regulator of glucose homeostasis has been demonstrated (7; 26). GLP-1 is released from L-cells in the distal small bowel and colon, and it is the most potent incretin. In the pancreas GLP-1 regulates somatostatin and glucagon secretion, proinsulin biosynthesis, apoptosis and expansion of β cell mass (7). The role of GLP-1 in the pathogenesis of type 2 diabetes and obesity has been demonstrated. We hypothesize that lower concentrations of GLP-1 could foster the higher risk of AAs adolescents to develop type 2 diabetes and their increased vulnerability to the effects of obesity on glucose metabolism. However, our results cannot explain whether these differences in GLP-1 concentrations are due to race-related inborn mechanisms or a consequence of obesity itself or some related abnormalities.

It has been demonstrated that compared to leaner subjects, obese counterparts have lower GLP-1\textsubscript{total} and GLP-1\textsubscript{active} concentrations and lower GLP-1 response to exercise (27). Both abnormalities improved after gastric bypass (28) or significant weight loss (29). In our sample, racial differences in GLP-1 concentrations could not be fully explained by differences in adiposity, as the mean weight, BMI, and RBMI were comparable (Table 1).

Area under the curve (AUC) is a measure of total response and gives a good estimation of both magnitude and duration of the response to glucose load over time. However, AUC does not indicate which of these components (magnitude or duration) is more relevant. Total levels of GLP-1 (especially at later times during the OGTT) may reflect the interaction of different factors, including production, secretion and clearance. Fasting and 15-minute concentrations may more accurately reflect secretory response and should be evaluated in conjunction with AUC values. Early changes in GLP-1 concentrations may also be more relevant in regulating early insulin response to glucose load.

Another potential explanation for these racial discrepancies in GLP-1 concentrations may be insulin resistance. Rask et al. reported that in non-diabetic men with wide-ranging insulin resistance, the GLP-1 response to a mixed meal is impaired and it is related to the level of insulin resistance (27). The most insulin-resistant men had 56% lower GLP-1 levels at 15 minutes and 63% lower GLP-1 AUC values. Multiple linear regression analysis showed that insulin resistance, but
Racial disparity in GLP-1 not obesity, was an independent predictor of the decreased incretin response.

Hyperinsulinemia has been suggested as the mechanism by which insulin resistance down-regulates the EIA (30; 31). In support of this observation, we found that fasting GLP-1_active and GLP-1_active AUC exhibited a trend toward significant associations with CISI (r = +0.29, P = 0.07 and r = +0.31, P = 0.06, respectively). However, given that our sample AA and C adolescents had similar insulin sensitivity, it is unlikely that the observed racial discrepancies in GLP-1 concentrations could be fully explained by these mechanisms. Interestingly, GLP-1_total AUC correlated with glucose AUC (r = +0.39, P = 0.02) and subjects with IGM exhibited higher GLP-1_total AUC (P = 0.03). These findings support the hypothesis that in obese adolescents with IGM the interaction of mechanisms affecting GLP-1 secretion and degradation could act synergistically to lead to the development of abnormal glucose metabolism.

Both obesity and insulin resistance have been found to be related to sub-clinical inflammation (15; 32). In agreement with other investigators, we found that the levels of fibrinogen were higher in AAs, and subjects with higher grades of inflammation exhibited higher BMI (P = 0.008), RBMI (P = 0.007), lower fasting GLP-1_active, and lower GLP-1_active-AUC (P = 0.004 and 0.046, respectively). Furthermore, fasting GLP-1_active negatively correlated with fibrinogen (r = -0.31, P = 0.03) and there was a trend toward significant association between fibrinogen and GLP-1_active AUC (r = -0.28, P = 0.07). This suggests that lower GLP-1_active in AAs could partially be explained by a racial predisposition to enhanced sub-clinical inflammation (15) and obesity, both of which could affect GLP-1 secretion or degradation.

We hypothesize that a potential mechanism by which obesity and inflammation could affect GLP-1 degradation is by enhancing the expression or activity of dipeptidyl peptidase IV (DPP-IV). DPP-IV is a type II integral membrane serine protease that is widely distributed throughout the body (33). Human DPP-IV cleaves N-terminal amino acids and inactivates the incretin hormones. It inactivates GLP-1 by > 50% in approximately 1 - 2 min, and 50% of the gastric inhibitory polypeptide (GIP) within 7 min. (33; 34). The expression of DPP-IV is ontogenetically controlled and developmentally regulated during thymocyte maturation (33; 35). It is known that DPP-IV is involved in a bimodal modulation of immune functions, mainly via expansion of T-cell activation but also by an inhibitory effect on corticosteroid release and chemokine inactivation. The net effect of DPP-IV activity could also explain the shift toward Th1 cytokine response (pro-inflammatory) through degradation of the cytokines involved in the Th2-like response (anti-inflammatory) (33).

Some limitations of the current study preclude us from making conclusive inferences. First, our small sample increases the potential risk of underestimating the magnitude and statistical significance of racial disparities in enteroinsular activity. For instance, as compared with AAs, C adolescents showed a 2.6 times higher GLP-1_active-AUC; however, this marked difference only reached marginal statistical significance (P = 0.06). Studies with larger samples of adolescents can help to reduce the chance of making type II errors. The use of BMI and RBMI as surrogate markers of adiposity and lack of information concerning exercise and dietary intake could represent potential confounders. There were also technical and reporting limitations that may affect the applicability of our results, including the lack of similar commercially available assays to assess active and inactive GLP-1 components. At present, GLP-1_active (GLP-1_7-37, GLP-1_7-36) is measured by ELISA using a specific N-terminal region monoclonal antibody, while
GLP-1_{total} (degraded GLP-1_{9-37}, GLP-1_{9-36}) is determined using a specific C-terminal antibody RIA that binds to the C-terminal portion of GLP-1. This limitation in methodology may foster variability and may not permit a clear comparison to quantify secretion and degradation. Similarly, there are no commercially available methods to assess the expression and activity of DPP-IV. We believe that the use of statistical methods like AUC help to overcome these limitations because AUC provides a better estimation of the discrepancy in the total response to glucose. Likewise, early changes in the response (during the first 15 min) may be a more accurate indicator of secretion capacity than levels at later times, which may be more affected by either kidney or liver extraction.

Our findings might have relevance concerning the potential deployment of emerging GLP-1-based anti-diabetic agents across ethnicities. Further studies will be needed to address the implications of disparities in GLP-1 levels in responses to anti-diabetic agents in subjects from different racial/ethnic backgrounds.

In summary, obese adolescents have a profound deterioration of insulin sensitivity and a higher prevalence of IGM and sub-clinical inflammation. Severity of overweight seems to be a major determinant in the development of such conditions. At comparable levels of overweight and insulin resistance, obese AA adolescents exhibit higher concentrations and prevalence of inflammatory markers, and lower concentrations of GLP-1_{active} and GLP-1_{total} than C peers. We hypothesize that these disparities may act in concert to foster the deterioration of glucose homeostasis in obese AA adolescents, and that these findings might be relevant to effective deployment of emerging GLP-1-based anti-diabetic agents across ethnicities.

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REFERENCES

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**TABLE 1.** Demographics and clinical characteristics of African-American and Caucasian study subjects

<table>
<thead>
<tr>
<th></th>
<th>AA (n = 37)</th>
<th>C (n = 12)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>14.1 ± 0.3</td>
<td>14.0 ± 0.7</td>
<td>0.75</td>
</tr>
<tr>
<td>Female (%)</td>
<td>78%</td>
<td>50%</td>
<td>0.08</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100.0 ± 3.4</td>
<td>91.6 ± 8.1</td>
<td>0.27</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>37.0 ± 1.2</td>
<td>33.2 ± 2.1</td>
<td>0.88</td>
</tr>
<tr>
<td>RBMI (%)</td>
<td>188.1 ± 5.8</td>
<td>170.3 ± 9.5</td>
<td>0.16</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>126.5 ± 1.9</td>
<td>119.3 ± 4.3</td>
<td>0.17</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>68.7 ± 1.1</td>
<td>65.2 ± 2.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Abnormal BP (%)</td>
<td>24 (65%)</td>
<td>4 (33%)</td>
<td>0.09</td>
</tr>
<tr>
<td>IGM (%)</td>
<td>15 (42%)</td>
<td>2 (17%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Inflammation (%)</td>
<td>30 (83%)</td>
<td>6 (50%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

BMI, body mass index; RBMI, relative body mass index; IGM, impaired glucose metabolism; ABP, abnormal blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure. All values expressed as least-squares mean ± SEM, except percentages. Analyses included ANOVA, ANCOVA and Fisher’s exact test. P values < 0.05 were significant and values ≤ 0.10 were considered as a trend.
**TABLE 2.** Insulin indices, inflammatory markers and enteroinsular axis measures by race$^a$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Sample (n = 49)</th>
<th>AA (n = 37)</th>
<th>C (n = 12)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>93.7 ± 1.7</td>
<td>93.9 ± 2.3</td>
<td>93.3 ± 1.5</td>
<td>0.84$^b$</td>
</tr>
<tr>
<td>Glucose AUC</td>
<td>14503 ± 373</td>
<td>14434 ± 503</td>
<td>14681 ± 371</td>
<td>0.80$^b$</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>37.2 ± 2.6</td>
<td>37.9 ± 3.0</td>
<td>35.3 ± 5.2</td>
<td>0.60$^b$</td>
</tr>
<tr>
<td>Insulin AUC</td>
<td>22493 ± 2932</td>
<td>23160 ± 3775</td>
<td>20736 ± 4033</td>
<td>0.70$^b$</td>
</tr>
<tr>
<td>ΔI30/ΔG30</td>
<td>5.9 ± 0.8</td>
<td>6.43 ± 0.98</td>
<td>4.75 ± 0.96</td>
<td>0.50</td>
</tr>
<tr>
<td>CISI</td>
<td>1.68 ± 0.15</td>
<td>1.54 ± 0.14</td>
<td>2.03 ± 0.43</td>
<td>0.30</td>
</tr>
<tr>
<td>CRP$_{hs}$ (mg/dl)</td>
<td>3.2 ± 0.6</td>
<td>3.52 ± 0.77</td>
<td>2.34 ± 0.77</td>
<td>0.90</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>391 ± 10.2</td>
<td>407.8 ± 10.5</td>
<td>343.2 ± 21.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Fasting GLP-1$_{total}$ (pM)</td>
<td>13.0 ± 1.0</td>
<td>12.75 ± 1.14</td>
<td>13.75 ± 2.5</td>
<td>0.70$^b$</td>
</tr>
<tr>
<td>15 min GLP-1$_{total}$ (pM)</td>
<td>19.8 ± 1.5</td>
<td>18.5 ± 1.7</td>
<td>23.5 ± 3.0</td>
<td>0.15$^b$</td>
</tr>
<tr>
<td>GLP-1$_{total}$ AUC</td>
<td>1526 ± 128</td>
<td>1333 ± 108</td>
<td>2034 ± 333</td>
<td>0.01$^b$</td>
</tr>
<tr>
<td>Fasting GLP-1$_{active}$</td>
<td>4.1 ± 1.2</td>
<td>3.31 ± 1.14</td>
<td>6.67 ± 3.84</td>
<td>0.30$^b$</td>
</tr>
<tr>
<td>15 min GLP-1$_{active}$ (pM)</td>
<td>5.3 ± 1.2</td>
<td>3.75 ± 0.63</td>
<td>9.5 ± 4.5</td>
<td>0.03$^b$</td>
</tr>
<tr>
<td>GLP-1$_{active}$ AUC (pM)</td>
<td>538 ± 142</td>
<td>374 ± 55.9</td>
<td>972 ± 490</td>
<td>0.06$^b$</td>
</tr>
</tbody>
</table>

$^a$All values expressed as mean ± SEM except percentages. Mean values of CISI, ΔI30/ΔG30, fibrinogen and CRP$_{hs}$ were adjusted by RBMI from ANCOVA and are least-square means. $^b$P values from Student’s t test except for CISI, ΔI30/ΔG30, fibrinogen and CRP$_{hs}$ which were taken from ANCOVA. P values < 0.05 were significant and values ≤ 0.1 were considered as a trend.
FIGURE LEGEND

Figure 1. Basal and stimulated concentrations of GLP-1_{active} (A) and GLP-1_{total} (B) during the oral glucose tolerance test (OGTT, 75 g glucose load during 2 hr test) in obese adolescent African-Americans (μ) and Caucasians (ο). For GLP-1_{active} AUC \( P = 0.06 \), and for GLP-1_{total} AUC \( P = 0.01 \).
FIGURE 1

[Graph showing active GLP-1 mean (pM) over time (Fasting min 15, min 30, min 60, min 90, min 120).

[Graph showing GLP-1 Total Mean (pM) over time (Fasting min 15, min 30, min 60, min 90, min 120).]