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Obesity in Caucasian T2D patients associates with higher levels of leptin and inflammatory cytokines: This is not the case in mestizo T2D patients

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Introduction: Recently we published on a set of T2D-related cytokines, chemokines and growth factors (TNF α , IL-1 β , IL-6, HGF, PAI, Resistin, CCL2, Adiponectin, Leptin, IL-8 and CCL4) measured in the serum of mestizo (Ecuadorian) T2D ambulatory patients and their respective non-diabetic controls. We only found IL-8 and HGF significantly raised in T2D patients versus the non-diabetic controls. We concluded that the mestizo T2D patients only showed mild signs of a raised inflammatory state in serum.

Aim: To test a set of T2D-related cytokines, chemokines and growth factors in the serum of comparable Caucasian (Dutch) and Mestizo (Ecuadorian) T2D patients with the same array system.

Methods: Using a commercially available multi analyte cytometric bead array system, the serum of age and gender comparable Ecuadorian and Dutch T2D cases and their respective non-diabetic controls were tested. Statistical analysis was performed using SPSS. Data was tested for normal distribution using the Kolmogorov-Smirnov test. Depending on the distribution pattern and the total number of subjects, nonparametric group comparison (Mann-Whitney U test) was applied. Correlations were determined by Spearman's correlation. Level of significance were set at $p=0.05$ (two tailed).

Results: The Dutch patients appeared to have a longer duration of T2D than the Ecuadorians (14 years vs. 6 years), they were slightly more hyperglycemic (HbA1C 8.4% vs. 7.3%) and they were somewhat more obese (BMI mean 31 vs. 28). The Dutch patients showed considerably higher serum leptin, pro-inflammatory cytokines (IL-6, TNF- α and IL-8) and HGF levels as compared to the Ecuadorian patients, who only showed mild signs of inflammation. Importantly, being obese in the Dutch patients was significantly associated with higher levels of leptin, while in the Ecuadorian patients this was not the case (Rotterdam $r=0.54$, $p=0.00$ vs. Ecuadorian $r=0.29$, $p=0.02$).

Conclusion: There are considerable differences in the leptin/adiponectin, pro-inflammatory cytokines and HGF serum profiles between age and gender comparable T2D patients from the Netherlands and Ecuador, the latter showing only mild signs of inflammation and no influence of the BMI on leptin, pro-inflammatory cytokine and HGF levels. Although the somewhat longer duration and the slightly higher hyperglycemia/BMI in Caucasian T2D cases might have played a role, it does not explain the absence of influence of obesity on leptin/HGF levels in the Mestizo cases as was typical of the Dutch patients. It is known from the literature that Amerindians have lower leptin production on the basis of genetic differences. It is also possible that juvenile infestations with helminths (typical in Ecuador) may have trained the innate immune system for anti-inflammatory responses in later life, thus preventing that obesity and particular macrophages in the fat induce a pro-inflammatory state in the T2D/metabolic syndrome.

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