Conclusions: A mildly elevated ZnT8 ab value with negative GAD-65, ICA, and IA values resulted in a severely progressed presentation of new onset Type 1 diabetes.
Studies have shown ZnT8 ab is more commonly associated with other positive diabetes abs, and less frequently found to be positive in isolation, particularly at a younger age. ZnT8 ab occurs in 3% to 4% of patients with type 1 diabetes who are negative for these other 3 abs. Use of the 4 abs results in 93% to 98% sensitivity encouraging routine Znt8 testing.
As De Grijse et al. noted, because ZnT8 is located within β-cell secretory granules, ZnT8A expression may not occur until there is enough β-cell damage to make ZnT8 immunologically visible. This may indicate that even low levels obtained during first-degree relative screens (e.g.Trialnet), could implicate imminent progression of diabetes.

P2-1852

ENDOGENOUS INSULIN SECRETION AND ITS RELATIONSHIP WITH HLA-MARKERS OF TYPE 1 DIABETES IN YOUNG CHILDREN

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Objectives: The residual endogenous insulin secretion influences on the clinical course of type 1 diabetes mellitus (T1DM). The aim of our study was to determine relationship of HLA genetic markers of T1DM and the C-peptide levels in young children with type 1 diabetes mellitus.
Methods: In order to elucidate the effect HLA-genotype on the residual function of pancreatic β-cells and the course of T1DM, 100 children, 50 boys and 50 girls aged 0.9 to 6.5 years were examined. The age of T1DM manifestation was 0.25 – 6.4 years (mean 2.7±1.1); before 1 year – 12 patients, 1-3 years – 64 patients, older than 3 years – 24 children. HLA-phenotype was detected by the standard lymphocytotoxical test. 59 HLA antigens classes I and II (A, B, DR, DQ loci) were taken into consideration. Basal and postprandial (60 and 120 minutes after standard breakfast) C-peptide levels was assessed by radioimmunoassay.
Results: The pancreatic insulin-secretory function was dramatically reduced in young children with T1DM. The mean value of basal C-peptide was 0.13±0.01 nmol/l. The residual secretion of insulin was revealed in 56.2% of children. "C-peptide-positive" patients accounted for 79.6% if duration of diabetes was less than 1 year; 46.2% - if duration of T1DM was 1-2 years; 33.7% - if duration of T1DM was 2-3 years; 20.0% - if duration of T1DM was 3-4 years; 16.7% - if duration of diabetes was more than 4 years.HLA-markers of predisposition to T1DM in early childhood were revealed: DQw3, DR3/4, DR4, DR3, B8. The HLA-markers of high risk of T1DM DR3, DR4 and moreover, DR3/4, as well as the age the diabetes onset and duration of disease were found to influence on the C-peptide level and duration of function of β-cells.

Conclusions: Our study shown that insulin-secretory function strongly reduced in young children with T1DM. We found HLA markers of high risk of T1DM in children: HLA - DR3/4, DR3, DR4, DQw3, B8. HLA- DR3, DR4 and moreover, DR3/4, as well as the age the diabetes onset and duration of disease to influence on the residual function of pancreatic β-cells.

POSTER SESSION 2
Friday, September 15, 2017, 11:30am-12:30pm
P2 - Type 2 diabetes and other carbohydrate metabolism
P2-1900 – P2-1906

P2-1900

INSULIN DYNAMIC AFTER THE STANDARD GLUCOSE LOAD AS A DIABETES MARKER IN OBESE ADOLESCENTS

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Objectives: Insulin resistance is recognized as a key pathogenic element of metabolic syndrome. Clinically we faced the problem when severely obese insulin resistant subjects are still below glycemic threshold for DM2 diagnosis. We hypothesized that post-load insulin response is the more valid marker of the diabetic beta-cell dysfunction than glucose response.
Methods: 64 adolescents aged 13,56 ± 2,47 y.o. with different BMI were examined. The laboratory assessment included fasting glucose and insulin measurement followed by standard oral glucose tolerance test. HbA1C greater than 6.5 % used for grouping for HbA1C "negative" (gr.1) and HbA1C "positive" (gr.2) subjects. Fasting insulin sensitivity assessed by HOMA-IR, QUICKI and whole body insulin sensitivity by Matsuda. Results were analyzed by using StatSoft Statistica 10.
Results: HbA1C level was 7.29 % in HbA1C "positive" vs. 5.75 % in HbA1C "negative" ($p<0.001$). HbA1C "positive" had higher Z-BMI (2.28±1.3 vs. 1.04±1.67, $p<0.025$) and waist toheight ratio (0.58±0.13 vs. 0.46±0.1649, $p<0.05$) with no gender and age differences.
HbA1C "positive" subjects had greater HOMA-IR (7.24±2.46 vs. 5.02±3.93, $p<0.001$), lower QUIKI (0.28±0.016 vs. 0.32±0.049, $p<0.001$) and lower Matsuda (2.09±0.77 vs. 4.88±0.72, $p<0.001$).
There was no difference in glycemic curve. Meantime, the insulin curve was statistically different in groups: fasting - 22.89±16.53 vs. 34.47±12.38; at 90 min - 60.33±36.82 vs. 99.38±33.61 ($p<0.025$); mean 56.38±24.37 vs. 73.15±19.99 ($p<0.025$).
Some parameters of insulin curve are highly specific for gr.1: no insulin decrease (or the second peak) after 60-th min (Se =

80.95%; Sp= 76.6%) and insulin min-max variability less than 200% (Se = 80.95%; Sp= 86.6%) with PPV=69.57% NPV=85.19 %. Usage of both Sp=96.6% and Se=96.3%.
Conclusions: HbA1C "positive" subjects have greater BMI and abdominal adiposity with more deteriorated both fasting and whole body insulin sensitivity.
The insulin curve after the standard glucose load in HbA1C "positive" obese adolescents differs even despite of the absence of diabetic blood glucose level.
Low insulin variability with no decrease (or second peak) after 60 min could be considered as markers of diabetes and indications for pharmacological interventions in obese adolescents.

P2-1901

INSULIN SENSITIVITY AND ß-CELL RESPONSIVENESS IN OBESE EUROPEAN CHILDREN AND ADOLESCENTS

Christian Denzer, MD; Katja Kohlsdorf, MD; Julia Von Schnurbein, MD; Martin Wabitsch, Professor; Josef A. Vogt, PhD, University Medical Center Ulm, Ulm, Germany

Objectives: Prevalence rates of T2DM in obese children and adolescents are significantly lower in European countries compared to the United States. Published data from cohorts of obese children and adolescents living in the US suggest a concurrent worsening of insulin sensitivity and ß-cell function over the spectrum of glucose homeostasis. If these results can be applied to European populations is currently unknown.
Methods: We recently proposed a novel method for mathematical modelling of insulin secretion and disposal from 3h, 8 sample OGTT data in children and adoelscents (Vogt et al., Am J Physiol Endocrinol Metab. 3111:E82-94, 2016). Here we combine our approach with a minimal model of glucose in order to estimate insulin sensitivity SI, ß-cell responsiveness Phi, and the disposition index DI (SI x Phi) in a population of n=133 (n=67 girls) obese children and adolescents (mean age 13.5 years (range 6.3 to 20.4 years), mean BMI z-score 2.83 (range 1.36 to 4.61).
Results: Of the total study population, n=4 subjects were diagnosed with impaired fasting glucose, and n=10 subjects had an impaired glucose tolerance. Regrouping the study population into tertiles of fasting glucose (t1: 61-81 mg/dl, t2: 82-87 mg/dl, t3: 88-113 mg/dl) and tertiles of 2h-glucose (t1: 56-97 mg/dl, t2: 98-115 mg/dl, t3: 116-190 mg/dl), respectively, revealed the following: SI decreased significantly over tertiles of fasting glucose and 2h-glucose (each $p<0.035$), whereas Phi remained unchanged over each category. Concordantly, the disposition index DI decreased significantly with increasing tertiles of fasting glucose (t1-t3: -32%) and 2h-glucose (t1-t3: -66%, each $p<0.03$). Adjusted for age, sex, pubertal stage, and BMI z-score, decreases in SI reached only borderline significance in the highest compared to the lowest tertile of fasting glucose ($p=0.064$). After adjustments, SI, Phi, and DI remained unchanged over tertiles of 2h-glucose.
Conclusions: In our cohort, increasing levels of fasting glucose and 2h-glucose were predominantly associated with worsening of insulin sensitivity but not declining ß-cell function. This observation may provide a pathophysiological explanation for the comparably low prevalence of T2DM in obese adolescents in Middle Europe compared to obese adolescents from multiethnic backgrounds in the US.

P2-1902

INVESTIGATING POTENTIAL ASSOCIATIONS BETWEEN HBA1C AND BLOOD PRESSURE IN ADOLESCENTS WITH TYPE 2 DIABETES MELLITUS

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Objectives: Type 2 Diabetes Mellitus (T2D) during adolescence is associated with childhood obesity. There is limited information about T2D associated co-morbidities in adolescents and the potential impact of these conditions on glycemic control. To investigate potential changes from diagnosis to first follow-up in HbA1c and blood pressure in adolescents with T2D.
Methods: This is a longitudinal retrospective analysis of 96 adolescents aged 10-17 years diagnosed with T2D at Children's Hospital of Michigan. Demographics and other variables including HbA1c, systolic and diastolic blood pressures (SBP and DBP) were analyzed at diagnosis and first follow-up clinic visit. SBP and DBP were classified as normal (NBP), prehypertensive (PHTN), or hypertensive (HTN) based on norms for age, sex, and height.
Results: Mean age was 14.4±1.9 years at baseline. The cohort was 65.6% female and 81.3% African American. Mean BMI was 37.1±11.7 kg/m^2. 93.7% had a family history of T2D. Follow-up at mean 4.8 months showed a decrease in HbA1c from 11.0±2.9% to 8.1±2.2% ($p\leq0.001$), a decrease in DBP from 72.1±8.5mmHg to 68.0±8.5mmHg ($p\leq0.01$) and an increase in SBP from 122.3±12.0mmHg to 126.7±13.1mmHg ($p\leq0.01$). 46.4% [95% CI 0.36, 0.57] of patients had SBP in the NBP range at baseline compared to 24.7% [95% CI 0.16,0.35] at follow-up; 28.6% [95% CI 0.20-0.39] had SBP in the PHTN range at baseline compared to 25.9% [95% CI 0.18,0.36] at follow-up; 25.0% [95% CI 0.17,0.35] had SBP in the HTN range at baseline compared to 49.4% at follow-up. HbA1c change from baseline to follow up was analyzed by follow-up SBP category: NBP -3.40$\pm$0.54 [95% CI -4.47,-2.33]; PHTN -3.85$\pm$0.53 [95% CI -4.89,-2.80]; HTN -2.18$\pm$0.38 [95% CI -2.93,-1.43]. The mean HbA1c difference between PHTN and HTN range was significant, -1.67$\pm$0.65 ($p=0.04$). There was no significant difference in mean HbA1c difference between groups with NBP versus HTN, -1.22$\pm$0.66 ($p=0.20$), or PTHN 0.45$\pm$0.75 ($p=1.00$), which may be due to sample size.
Conclusions: There is a possible association between hypertensive blood pressures and smaller improvements in HbA1c.