Poster Tour 1 - Diabetes and Epidemiology

P-68-001

Two-bag system in the management of diabetic ketoacidosis: experience of from a tertiary care hospital in Pakistan

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Background: Management of Diabetic Ketoacidosis (DKA) requires frequent changes of intravenous fluids in response to fluctuating needs of electrolyte, and dextrose. Abrupt changes in electrolytes and glycemia can lead to cerebral edema in DKA. The ''two-bag'' system can prevent these abrupt changes.
Objective: To present experience of Diabetic Ketoacidosis (DKA) management in children using ''Two Bag System'' from a developing country.
Study design: Retrospective chart review.
Setting: Aga Khan University Hospital (AKUH), Pakistan.
Subjects: Children 0–15 years of age, admitted with diagnosis of DKA at AKUH from June 2006 to June 2011.
Methods: Files of all subjects were reviewed. The diagnosis of DKA was based on established international criteria. The time for resolution of acidosis was taken from the start of treatment to reach a venous pH of 7.30 or better. The cost of IV therapy for each bag, and the possible time delays if bags were changed were calculated with help from pharmacy services.
Results: Total of 76 children were admitted with the diagnosis of DKA. Mean age of 7.3 ± 4.7 years. There were 36 (47.4%) boys and 40 (52.6%) girls. Newly diagnosed cases were 49 (64.5%). 23 (30.3%) cases had mild, 22 (28.9%) moderate and 31 (40.8%) had severe DKA. There were no episodes of hypoglycemia after initiation of therapy. The mean time for acidosis correction was 19.7 hours. There were no deaths in the study group. The time lag for changing the glucose concentration of infusion was 5 minutes after glucose check against a possible 1 hour if new bags were ordered. Cost of fluid therapy was approx. 30 ± 5 $ for two bag system against a possible 50 ± 5 $ if it was not used.
Conclusions: The two-bag system enables faster fluid therapy changes, allowing a steady and gradual fall in blood glucose after start of insulin therapy in DKA. It is also cost effective and decreases the work for pharmacy and nursing staff.
Keywords: Diabetic Ketoacidosis, Two-bag system, Paediatrics.

P-420-002

A human cardiovirus, Saffold virus, does not seem to be associated with type 1 diabetes

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Objectives: Cardiovirus infections in rodents have been implicated in the development of type 1 diabetes (T1D). Recently a novel picornavirus, Saffold virus (SAFV), was identified as the first human cardiovirus. We wanted to test whether SAFV is associated with the development of persistent islet autoantibodies in children with the high-risk HLA genotype. This is the first large-scale study to test for SAFV in a case-control cohort for T1D.
Methods: Individuals carrying the HLA-DRB1*04:01-DQA1*03-DQB1*03:02/DRB1*03-DQA1*05-DQB1*02 genotype were identified at birth and followed with monthly stool samples from age 3 to 35 months. Blood samples taken at 3, 6, 9, 12 months of age, and then annually, were tested for autoantibodies to insulin, glutamic acid decarboxylase 65 and protein tyrosine phosphatase-like protein IA-2. Among 911 children, 27 developed positivity for ≥2 islet autoantibodies in ≥2 consecutive samples (cases). Two controls per case were matched by follow-up time, date of birth and county of residence. Stool samples were analyzed for SAFV with a semiquantitative real-time reverse transcriptase PCR.
Results: Preliminary analyses show that 30 of 939 (3.2%) samples were positive for SAFV RNA, with no difference between cases and controls. There was a seasonality with higher risk from November to January. The estimated relative risk for islet autoimmunity and SAFV RNA positive sample during follow-up was 1.48, 95% CI: 0.34–6.51, P = 0.601. The viral quantities ranged up to approximately 1 x 10^5 copies, with no difference observed between cases and controls.
Conclusions: In this first large scale study of SAFV in fecal samples from infants and toddlers approximately 3% of longitudinal fecal samples were positive, but we did not find any significant association with the development of persistent islet autoantibodies. Larger studies should be done to rule out weak to moderate associations, but our preliminary results suggests that strong effects are unlikely.

P-143-003

Spatial distribution and time trend of type 1 diabetes mellitus in children in North Rhine-Westphalia, Germany

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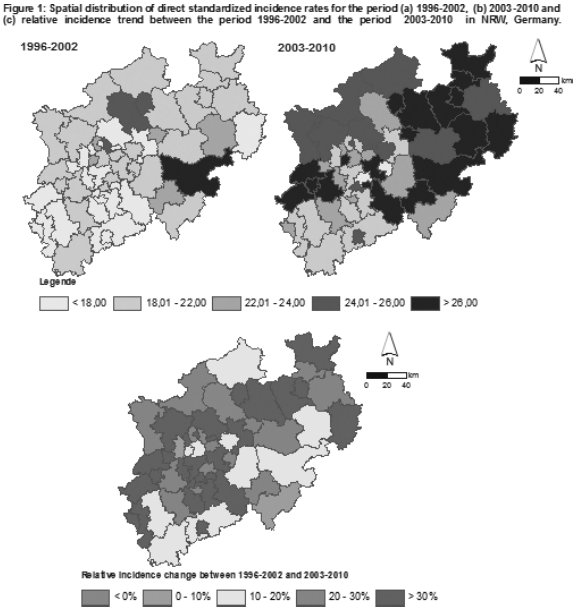
Objective: The objective of the present study was to analyze the spatial distribution and time trend of the incidence of type 1 diabetes (T1DM) in children <15 J between 1996 and 2010 in North Rhine-Westphalia NRW, the most populous German federal state. This study aimed to identify risk areas of major increase in the incidence of T1DM.
Methods: Data source was the NRW diabetes incidence register. Incidence and confidence interval (95%-CI) were calculated per 100 000 person-years based on Poisson distribution. Completeness of ascertainment was estimated by the capture recapture method. Age- and sex-standardized incidences were estimated by the direct method in two periods (1996–2002, 2003–2010). The spatial variation of the incidence was evaluated by means of the direct standardized incidence rates and the local Moran's I coefficient LISA.
Results: 9165 cases with incident T1DM were registered in NRW in 1996–2010. Of these, 53% were boys. Completeness of ascertainment was 98.6%. The incidence rate rose from 19.1 to 24.4 (per 100 000 person-years) between the two periods, indicating an increase of about 28% The incidence estimates differed between evaluation periods, age-groups and sexes.

During 1996–2002, the incidence in boys [girls] in the age-group 0–4, 5–9 and 10–14 was 13.8 (12.6–15.2) [12.3 (11.1–13.6)], 20.6 (19.2–22.2) [20.8 (19.3–22.4)], 23.4 (21.8–25.0) [23.3 (21.7–25.0)], respectively. During 2003–2009, respective incidences were 18.0 (16.6–19.5) [17.9 (16.4–19.4)], 26.6 (25.0–28.4) [28.6 (26.8–30.4)], 31.4 (29.7–33.2) [24.0 (22.5–25.7)]. The greatest increases in T1DM over time were found in the south-western district of NRW (Fig 1). The hotspot was associated with densely populated districts.
Conclusion: This study demonstrates both spatial and temporal heterogeneity of the incidence of T1DM pointing to the important role of environmental factors in the disease aetiology. Further, this information can contribute to the optimization of the diabetes healthcare planning.



P-344-004

Seasonal variation in month of diagnosis in children with type 1 diabetes registered in 23 EURODIAB centres during 1989-2008

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Objectives: To investigate seasonal variation in month of diagnosis in children with type 1 diabetes registered in EURODIAB centres during 1989–2008.
Methods: Twenty-three population-based registers recorded date of diagnosis in new cases of clinically diagnosed type 1 diabetes in children aged under 15 years. Completeness of ascertainment was assessed through capture-recapture methodology and was high in most centres. A general test for seasonal variation (11*df*) and Edward's test for sinusoidal (sine wave) variation (2*df*) were employed. Time series methods were also used to investigate if meteorological data were predictive of monthly counts after taking account of seasonality and long term trends.
Results: Significant seasonal variation was apparent in all but two small centres, with an excess of cases apparent in the winter quarter. Significant sinusoidal pattern was also evident in all but two small centres with peaks in December (14 centres), January (5 centres) or February (2 centres). Relative amplitude varied from ±11% to ±39% (median ±18%). There was no relationship across the centres between relative amplitude and incidence level. However there was evidence of significant deviation from the sinusoidal pattern in the majority of centres. Pooling results over centres, there was significant seasonal variation in each age-group at diagnosis, but with significantly less variation in those aged under 5 years. Boys showed marginally greater seasonal variation than girls. There were no differences in seasonal pattern between four sub-periods of the 20 year period. In most centres monthly counts of cases were not associated with deviations from normal monthly average temperature or sunshine hours; short term meteorological variations do not explain numbers of cases diagnosed.
Conclusions: Seasonality with a winter excess is apparent in all age-groups and both sexes, but girls and the under 5s show less marked variation. The seasonal pattern changed little in the 20 year period.

P-266-005

Diabetic ketoacidosis at diagnosis in Austrian children-a population based analysis 1989–2011: no reduction by a community based campaign

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Objectives: Diabetic ketoacidosis (DKA) is a life-threatening complication of type 1 diabetes. Recent investigations reported a decrease of onset DKA by special information campaigns or by prevention programmes. The aim of the study was to analyse

the effect of a public information programme on the frequency of onset DKA in Austria.
Methods: In a prospective population based incidence study all newly diagnosed patients with diabetes ≤15 years of age were registered by the Austrian Diabetes Incidence Study Group. Registered data: BG, pH, ketonuria and clinical symptoms of DKA. DKA was defined as pH <7.3, severe DKA as pH <7.1. Data between 1989 and 2011 were available. In autumn 2009 a community based intervention programme similar to the Parma Campaign was initiated (40 000 posters in schools, kindergartens, medical practices, pharmacies).The frequency of onset DKA in the years 2005–2009 and 2010–2011 was compared. Difference in DKA prevalence between time periods as well as time trends were tested by Chi-Squared test and logistic regression.
Results: During the study period 4033 children were registered. 37% presented with DKA, 26% had a mild and 11.5% a severe form. The frequency of DKA was negatively associated with age at onset. In the years before the intervention programme 26% of newly diagnosed children presented mild DKA compared to 27% after the intervention. The prevalence of severe DKA in the years before the campaign was 12% compared to 9.5% thereafter (n.s.). No significant change in the onset DKA rate by the intervention programme could be found comparing the age groups <5, 5 to 10 and 10 to 15 years, neither for mild nor for severe DKA.
Conclusions: The frequency of DKA in children with newly diagnosed type 1 diabetes in Austria is still high and did not change despite a clear increase in the manifestation rate. Efforts to reduce the occurrence of onset DKA by a community information programme were not successful.

P-394-006

Vitamin D levels in youth with type 1 diabetes: effects of vitamin D supplementation on glycemic control

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Background: Vitamin D influences β cell function and is reported to rise insulin efficacy in type 2 diabetes (T2D) but there aren't studies that define a similar relationship in type 1 diabetes (T1D).
Objectives: This prospective, non controlled, study aims
(i) to investigate vitamin D levels in pediatric patients with T1D and
(ii) to establish if a correlation between serum vitamin D levels and glycemic control does exist.
Methods: A total of 298 patients with T1D were included in the study. 25-hydroxyvitamin D (25OHD) serum concentration, hemoglobin A1c levels (HbA1c) and insulin requirement were evaluated at baseline and after 11 ± 4 months. Vitamin D deficiency and insufficiency were defined as a 25OHD concentration <20 ng/ml and 21–29 ng/ml respectively. Patients who had 25OHD levels <30 ng/ml were assigned to receive 600 IU of vitamin D daily. The Student's *t*-test was used to compare the results expressed as mean ± SD and values of $P < 0.05$ were considered significant.
Results: Vitamin D deficiency was present in 43.9% of patients and insufficiency in 35.5%, according to studies conducted on healthy children. Among 124 patients with inadequate 25OHD levels, who received vitamin D supplementation, 59.7% showed increased 25OHD levels, 40.3% decreased or unchanged 25OHD levels. Children who showed increased 25OHD levels achieved a significant HbA1c decrement, up to - 0.47% when 25OHD values increased of at least 5 ng/ml ($P = 0.03$). Insulin requirement in these patients decreased after vitamin D supplementation (-0.18; $P = 0.34$). No differences in HbA1c were found among subjects with decreased or unchanged 25OHD serum levels.
Conclusions: We observed that vitamin D supplementation is associated with an improved glycometabolic control in children with T1D and hypovitaminosis D. Since only 20% of children with T1D show 25OHD adequate serum levels we recommend checking 25OHD levels in children with T1D and starting treatment if they are deficient/insufficient.

P-430-007

AADE 7 behaviors in a type 1 diabetes pediatric population

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Introduction: The American Association of Diabetes Educators (AADE), through evidence-based medicine, showed there are seven behaviors that may indicate the state of health of the diabetic patient, and they can also guide the educator to change patient's behaviors that need to be improved. Such behaviors are healthy eating, being active, monitoring, taking medication, problem solving, healthy coping and reducing risks.
Objective: To evaluate the AADE seven behaviors in pediatric type 1 diabetes (T1DM) population enrolled in our service.
Methods: We analyzed 191 T1DM patients, under 18 years old, through a cross-sectional study submitted to a questionnaire, along with single anthropometric measures and laboratory work-up.
Results: The average age of the population was 10.9 years, 54% of them were >11 years old. The average age at diagnosis was 5.2 years; and the average time from illness was 5.6 years. Twenty two percent of them were overweight and 15% were obese: 39% did not practice any type of physical activity. Seventy six percent of the population performed four or more SMBG per day; but only 9% of them used four or more correction bolus of insulin. Of the patients, 95% used NPH insulin; 31% of them performed two applications and 64% three applications; 72% were rapid-acting insulin users and 23% were short-acting insulin users. Fifty five percent showed HbA1c up to 9%; 31% between 7.6 and 9%; and 14% under than 7.5%. The age was directly proportional to HbA1c. Three percent were smokers or former smokers. Two percent users or former users of illicit drugs. None of them reported daily use of alcoholic beverage. Nine percent were admitted in a E.R unit with ketoacidosis, and 56% of those had HbA1c greater than nine.
Conclusion: The studied population still needs many orientation guidelines for making behavior changes in relation to diabetes. These data provide tools to begin a structured work of education that suits the individual needs of the patient.

P-268-008

Prevalence of asthma in children and adolescents with type 1 diabetes in Germany and Austria: no impact on metabolic control

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Objectives: The prevalence of asthma in diabetic youth has been described to be increased and the concomitant diagnosis was

associated with poor metabolic control. The aim of the study was to estimate the prevalence of asthma in a large cohort of children and adolescents with type 1 diabetes and to analyze a possible impact on metabolic control.
Methods: In an observational cohort study based on the DPV-database (German/Austrian DPV initiative) data from 51926 patients (52% male) with type 1 diabetes (<20 years) could be analyzed. The mean age was 13.9 ± 4.2 years (mean ± sd) and the mean duration of diabetes 5.3 ± 4.2 years. All clinical data were documented prospectively in the DPV-data base. Data were analyzed using the SAS software. For group comparisons, non-parametric statistical tests and a linear regression model were used, with adjustment for multiple comparisons.
Results: 1755 (3.4%) of the whole cohort had the diagnosis asthma or received medical treatment for asthma. Patients with asthma used higher insulin doses (0.88 vs 0.84 IU/kg, P < 0.01) and were more often males (61 vs 52%, P < 0.01). We observed a lower height SDS (-0.11 vs -0.04, P < 0.05) and an increased BMI-SDS (0.56 vs 0.52, P 0.06). No significant difference was found for HbA1c between patients with and without asthma (8.27 vs 8.25%). 495 (28%) patients with asthma were treated with cortisone, 425 (24%) with sympathomimetic drugs, 104 (6%) used leukotriene receptor antagonists, 72 (4%) various other medications, while 659 (37%) were without pharmacotherapy .No relevant influence of the type of asthma medication on metabolic control or BMI-SDS could be found.
Conclusions: It seems, that the prevalence of asthma in children and adolescents with type 1 diabetes in Germany and Austria is not elevated. The diagnosis asthma and pharmacological treatment have no relevant influence on the metabolic control.

P-123-009

Characterization of pediatric patients with cystic fibrosis related diabetes (CFRD) compared to pediatric patients with type 1 diabetes (T1DM): an analysis based on a German/Austrian pediatric registry

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Background: The prevalence of cystic fibrosis-related diabetes (CFRD) has increased with improved life expectancy of CF patients. In order to better describe these patient group, clinical and care characteristics were compared to type 1 diabetes (T1DM) in a multicenter analysis of pediatric data.
Methods: Auxological and treatment data from 47 227 patients aged <21 years with CFRD (n = 381) or T1DM (n = 46.846) in the German/Austrian DPV registry were analyzed by multivariable mixed regression modeling. Results are indicated as median and interquartile range.
Results: Diabetes onset (mean [interquartile range]) occurred later in CFRD (14.5 [11.8–16.3] years) than in T1DM (8.5 [4.9–11.8] years), with female preponderance in CFRD (59.1% vs 47.5%, P < 0.01). CFRD patients had a lower BMI-SDS (-0.85 [-1.59 - -0.12] vs +0.52 [-0.10 - +1.16]; P < 0.01) and lower HbA1c (6.87% vs 7.97%, P < 0.01). Self monitoring of blood glucose was less frequent in CFRD (3.5 vs 4.5; P < 0.01). In contrast to T1DM, where all patients were treated with insulin, only 72% of CFRD patients received insulin therapy. In insulin treated patients, insulin dosage adjusted for age, sex and diabetes duration differed significantly (T1DM: 0.79 vs CFRD: 0.83 IE per kilogram bodyweight). Use of short and long acting insulin analogues was significantly less frequent in CFRD (39% vs 47% and 28% vs 37%, both P < 0.05).
Conclusion: Pediatric CFRD patients show clear auxological and metabolic differences from T1DM and there are different treatment choices.

P-178-010

Diabetic ketoacidosis at onset in children and adolescents with type 1 diabetes in Norway - a nationwide population-based cohort study

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Objectives: To determine the prevalence and severity of diabetic ketoacidosis (DKA) at onset in cases with type 1 diabetes (T1D) <15 years.
Methods: Prospective registration of all new cases of T1D (0–14 years) in the Norwegian Childhood Diabetes Registry (NCDR). Completeness of ascertainment in NCDR is >92%. DKA is defined as pH <7.3 or bicarbonate <15 mmol/l (1). The severity of DKA was categorized by the degree of acidosis (1): Mild: Venous pH <7.3 or bicarbonate<15 mmol. Moderate: pH <7.2, bicarbonate <10 mmol/l. Severe: pH <7.1, bicarbonate <5 mmol. In 2010, 292 patients were diagnosed with T1D, 57% male. Ten (3.4%) patients had missing DKA data, and were excluded, leaving 282 patients with complete data; 57% male, mean age 9.3 years (range 0.8–14.9).
Results: Fifty-one patients (17.5%) fulfilled the criteria of DKA; boys 17.0%, girls 18.3%. The proportions of patients with DKA at presentation of T1D by age were: 0–4 years 16.3%, 5–9 years 11.3%, age 10–14 years 21.9%. 41% of the patients had mild DKA, 35.3% had moderate DKA and 23.5% had severe DKA. The severity of DKA stratified into gender and age group is presented in Table 1.
Conclusion: The prevalence of children with DKA at onset of T1D is very low in Norway. The highest proportion of children with DKA was in the age group 10–14 years. The highest proportion of severe DKA was found in the youngest children (0–4 years). The risk of DKA at onset of T1D has been dramatically reduced in Norway, probably due to better knowledge of the disease in primary care and in the general population.
References: [1] ISPAD Consensus Guidelines 2009. Pediatric Diabetes 2009:10:118.

Table 1. Severity of DKA at presentation of T1D.

Age group (years)	Gender	Mild DKA %	Moderate DKA %	Sever DKA %
0–4 years	Male	40.0	0	60.0
	Female	0	33.3	66.7
5–9	Male	75.0	0	25.0
	Female	42.9	28.6	28.6
10–14	Male	36.8	47.4	15.8
	Female	46.2	46.1	7.7

*For the 40–80 mg/dl range, values are mean absolute differences in mg/dl. For other glucose ranges, values are expressed as mean absolute relative differences in %.

P-234-011

Incidence of type 1 diabetes mellitus in 0–14 year children and their demographic and clinical characteristics: first regional report from Turkey

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Objective: Epidemiological characteristics of type 1 diabetes mellitus (T1DM) are important because of variabilities in incidence of disease, which are related to region, ethnic, gender and age. There is no incidence study, which is performed in our region and also in Turkey in pediatric age group. Aim of present study was to define incidence, demographic and clinical characteristics of T1DM in 0–14 age children in Diyarbakir, one of the biggest cities of southeast region of Turkey.
Method: Data of all T1DM patients, diagnosed between dates 1 June 2010 and 31 May 2011, were evaluated. And 0–14 age group population data were obtained from Turkish Statistical Institute (TSI) for Turkey.
Results: From a total of 41 T1DM patients, 24(58.5%) were female (male: 41.5%) with a male/female ratio of 1.4. Disease incidence was $8.7/10^5$ in female and $5.7/10^5$ in males; overall annual incidence was $7.2/10^5$. Peak incidence in girls was at 5–9 years age group, and 10–14 years of age in boys. Total incidence in 5–9 and 10–14 years age groups were very close to each other (incidence rates were 9.1 and 8.4, respectively). Mean age of the diagnosis was 8.1 ± 4.6 years. Rate of presentation with diabetic ketoacidosis was 65.9%. Patients applied most frequently in spring and winter months (15 and 11 patients, respectively).
Conclusion: In this first incidence study on pediatric age group in Diyarbakir, T1DM incidence was similar to that of countries in low-middle incidence group.

P-282-012

Sever hypoglycemia and diabetic ketoacidosis among children with type 1 diabetes in a population based, nationwide cohort

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Objectives: Severe hypoglycemia (SH) and diabetic ketoacidosis (DKA) are the most problematic acute complications of type 1 diabetes (T1D) in youth. The Norwegian Childhood diabetes Registry (NCDR) includes 95% of all children with diabetes in pediatric departments in Norway. The aim of this study was to investigate the prevalence of DKA and SH in a nationwide, population based pediatric cohort.
Methods: Data obtained at the annual examination in NCDR in 2011 from 2476 participants with T1D. 19 cases (0.8%) were excluded because of missing data on DKA and SH, leaving 2453 patients with complete data; 53% male, mean age 12.9 years (range 1.7–19.0 years), mean diabetes duration 5.3 years (0.2–17.1), 95% Nordic ethnicity. Prevalence of DKA (defined as hospitalized with pH <7.3 or bicarbonate <15 mmol/l) and SH (defined as unconsciousness with or without seizure) in relation to gender, age and HbA1c were analyzed.
Results: DKA occurred in 4.8% (0.6% >1 event) and SH in 6.3% (1.3% >1 event) of the cases. Male: DKA 4.7% (0.5% >1 event), SH 6.5% (1.6% >1 event). Female: DKA 5.1% (0.7% >1 event), SH 6.3% (1.0% >1 event). The total proportion of cases with both DKA and SH events was 0.5% (males 0.3%, females 0.7%). Stratified into age groups <5, 5–9, 10–14 and ≥15 years it was 2.9%, 0.7%, 0.4% and 0.2% respectively. Prevalence of DKA and SH stratified by age and HbA1c is presented in table 1.
Conclusions: Children and adolescents with T1D in Norway has a rather low prevalence of DKA and SH. However, DKA and SH remain major challenges in youth with T1D. Significant less DKA in youth with HbA1c <7.5%.

Table 1. Prevalence of DKA and SH by HbA1c and age.

Age (years)	HbA1c <7.5% n = 632		HbA1c >8.5% n = 862		P	P
	DKA (%)	SH (%)	DKA (%)	SH (%)	DKA	SH
0–4	4.3	6.4	7.1	14.3	ns	ns
5–9	3.4	5.7	3.4	5.2	ns	ns
10–14	2.7	5.0	7.5	5.9	0.0085	ns
≥15	0.7	5.4	5.5	6.7	0.0124	ns

P-56-013

Working premises for preventing DKA at T1D onset in Romanian children

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Objectives: To present an analysis on our T1D onsets and describe the DKA prevention campaign we intend to implement.
Methods: We studied retrospectively demographic, clinical and biological data of children with T1D managed at onset in our hospital between 2003 and 2012. DKA was defined and classified by ISPAD guidelines.
Results: Our study population consisted of 99 children, mean age 9.7 years (range 1–17). 57.57% (n = 57) were boys. 63.63% (n = 63) of the children came from an urban area. The mean period of time between the onset of classic diabetes symptoms and the diagnosis was 28.58 days (range 1–180). 2 children didn't show the classic symptoms, their hyperglycemia being an incidental finding. From the 99 children, 57 (57.57%) presented with DKA and 26 (26.26%) had a severe form. Children that presented with DKA had a mean age of 9.96 years and a mean duration of symptoms of 24.04 days. Only one child was treated for cerebral edema. When we studied the yearly timeline we discovered that the frequency of both T1D onsets and the severe forms of DKA was high at the beginning of the studied period (15 cases in 2005, six with severe DKA), reached a low point between 2007 and 2009, and is on a rising slope for the last 2 years (13 cases in 2011, three with severe DKA). The low point coincided with the implementation of a national program that evaluated our population's health and included blood glucose testing.
Conclusions: Considering the high numbers of T1D onsets with severe DKA we are facing, we decided to start a national

prevention campaign similar to the Parma campaign. We designed posters to raise awareness about the classical onset symptoms of T1D and found sponsors for their printing. We intend to distribute them in schools, general practitioners' offices and hospitals' waiting rooms. We hope our campaign will be a success.

Poster Tour 2 - Diabetes and Epidemiology

P-307-165

Dietary habits and their associations with insulin sensitivity and insulin secretion in youth

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Objectives: Data on the associations between insulin dynamics and dietary macronutrient composition in youth are sparse, and often fail to adjust for other lifestyle habits. Our objectives were to examine the associations between macronutrients and insulin sensitivity (IS) and insulin secretion (ISct), taking into consideration moderate-to-vigorous physical activity (MVPA), fitness and sedentary behavior.
Methods: Caucasian youth ($n = 630$) aged 8–10 years at recruitment, with at least one obese biological parent, were studied (QUALITY cohort). IS was measured using HOMA-IR and Matsuda-ISI. ISct was measured using HOMA2%-beta, the area under the curve (AUC) of insulin to glucose over the first 30 minutes (AUC $I/G_{t30\ minutes}$) of the oral glucose tolerance test and AUC $I/G_{t120\ minutes}$ over 2 hours. Fitness was measured by VO_{2peak}; percent fat mass (PFM) was measured by DXA; 7-day MVPA was measured using accelerometry and screen time was assessed by average daily hours of self-reported television, video game or computer use (ST). Dietary composition was measured using 3 non-consecutive dietary recalls. Non-parametric smoothing splines were used to model non-linear associations; all models were adjusted for age, sex, season, and pubertal stage, MVPA, fitness, ST and adiposity.
Results: We considered daily total kilocalories, % protein, % fat, %saturated fat, % carbohydrate, vitamin D, sugar-sweetened beverages, fiber and portions of fruits and vegetables. No dietary component was associated with any measure of IS after adjusting for MVPA, fitness, ST and adiposity. For every 1% increase in daily %protein intake, AUC $I/G_{t30\ minutes}$ decreased by 1.1% ($P = 0.033$). Otherwise, dietary composition was not associated with ISct.
Conclusions: Dietary habits, above their established association with adiposity, are not correlated with IS and ISct overall. These findings suggest that strategies to prevent type 2 diabetes mellitus in youth should focus on increasing MVPA and decreasing screen time.

P-424-166

Diabetes behaviour and the outcome of diabetes in children and adolescents with T1D in Denmark in the period 2000–2011

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Objectives: Diabetes management has become more and more intensive over the last ten years in Denmark. Is it followed by the expected improved outcome?
Methods: A national register-based study including children and adolescents <17 years from Denmark diagnosed with Type 1 Diabetes (T1D) followed from 2000 till 2011 both year included. Clinical data was prospectively recorded, including events of severe hypoglycaemia (SH), annual glycated haemoglobin A1c (HbA1c) and treatment regime. SH was defined as unconsciousness and/or seizures and a blood glucose level of <3.5 mmol/l. Regression analysis taken the repeated measures into account were used to estimate the impact of behaviour on Hba1c.
Results: The percentage of children measuring more than six daily blood glucose values (SMBG) has increased from 5 to 35% from 2009 to 2011. The percentage of children treated with MDI injecting more than five boli a day has increased from 20 to 75% from 2007 to 2011. The percentage of children on pumps has increased from 0 to 50% from 2004 to 2011. In the period 2000–2006 Hba1c has decreased and since then it has stabilized around 8.3%, with no further improvement. Over the last four years the number of SH have decreased by 38% (SEM 5%, $P < 0.001$) annually. The increased number of SMBG and bolus is significantly associated with an improved HbA1c ($P < 0.001$), whereas there is no association between number of injections on MDI and HbA1c. The frequency of SH for patients on CSII compared to MDI is 32% (SEM = 13%, $P = 0.014$).
Conclusions: The intensified treatment has lead to a clinical relevant reduction in HbA1c, but have reached a plateau. Intensified use of the pump with more than six SMBG and five boli a day is associated with a better outcome. Pump treatment have reduced the number of SH substantially. The failure to find association between the number of injections on MDI probably reflects the difficulties in estimating the true number of injections on MDI treatment compared to pumps.

P-186-167

Epidemiological pattern of patients attended the Pediatric Outpatient Clinic of National Institute of Diabetes and Endocrinology, Cairo, Egypt

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Background: Diabetes mellitus is the most common endocrine metabolic disorder of childhood. It is widely spread all over Egypt as its prevalence was found to be 1.09 per 1000 among school aged children.
Aim: The aim of this work was to do a retrospective epidemiological study of the records of diabetic children attended the outpatient pediatric clinic in NIDE.
Subjects and methods: The files 0f 3000 diabetic children were examined retrospectively without any reference to the personal data.
Results: The results showed that there is no statistical differences between male, ($n = 1424$) to female, ($n = 1576$) distribution. The results of this retrospective study showed that the mean age of onset of diabetes in children attended the outpatient pediatric clinic of National Institute of Diabetes was (mea $n = 8.37 + 10.96$ years). The present study showed also that there was a decrease of age of onset of diabetes among diabetic children as the age of onset between 5 to <10 years were the highest percentage (46%). As regards the insulin regimen used by the diabetic children, 17.5% used conventional insulin therapy, 11% used modified insulin therapy as they used regular insulin before lunch, and 71.5% used basal-bolus insulin regimen. The mean percentage of insulin unites per Kg. was 1.00 + 0.38 U/kg/day. The results showed also that 34.8% of the diabetic patients were doing continues home blood glucose monitoring with glucose sensors, 25.8% were doing the monitoring only with visual strips, while 39.4% of the diabetic children were not doing home monitoring at all.

Conclusion and recommendations: The discussion of these results documented that it will be essential to follow the international guidelines of management of type 1 diabetes and it was recommended to study the prevalence and incidence of diabetes among Egyptian children as the prevalence and incidence still uncertain till now.

P-538-168

Ten year trend for diabetic ketoacidosis in children at diagnosis of type 1 diabetes from Brisbane

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Diabetic Ketoacidosis (DKA) (blood glucose >11 mmol/l with a venous pH <7.3 and/or bicarbonate <15 mmol/l) is a major contributor to morbidity and mortality in children with diabetes.

Objectives: Our aim is to identify and explore the trend of DKA among children (<18 years of age) at diagnosis from two major paediatric tertiary centres in Brisbane, (The Royal Children's Hospital (RCH) and Mater Children's Hospital (MCH)) for the 10 years 2001–2011.

Methods: Data for children presenting to the RCH with newly diagnosed Type 1 Diabetes Mellitus (T1DM) between January 2001 and December 2011 (n = 357, 186 were males) were retrospectively studied for the presence of DKA and analysed by gender, age group and year of diagnosis.

Results: 38.4% presented in DKA (n = 137), 50.4% No DKA (n = 180), 11.2% Unknown DKA (n = 40). There was no significant difference (P = 0.527) between gender in regards to DKA at diagnosis. Median age at diagnosis of children presenting with DKA was significantly lower than children without DKA (7.88, 9.13 P = 0.004) and the percentage of DKA cases was significantly different across the three age groups (<5 years 50.9%, 5–12 years 31.5%, >12 years 36.4%, P < 0.001). Data for children presenting to the MCH is currently available for 2010–2011 (n = 133, 73 were males). 51.1% (n = 68) of children presented in DKA with a Median age of 8.9. A higher proportion of younger children presented in DKA (<5 years 73.3%, 5–12 years 48.6%, >12 years 51.5%).

	Year of Diagnosis			Total
	2001-2003 n= , (%)	2004-2007 n= , (%)	2008-2011 n= , (%)	n=
DKA Yes	25 (37.9)	64 (41.6)	48 (35.0)	137
DKA No	25 (37.9)	75 (48.7)	80 (58.4)	180
DKA Unknown	16 (24.2)	15 (9.7)	9 (6.6)	40

Conclusion: The results show that a high proportion of children, particularly those <5 years, continue to present in DKA when initially diagnosed with TIDM. The incidence of DKA at diagnosis has not appreciably decreased over 10 years and highlights the need for an intervention to improve awareness of the common symptoms of T1DM.

P-474-169

Prevalence and incidence of type 1 diabetes among children aged 0–18 years in Samsun, Turkey

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Objectives: We aimed to determine the current incidence and prevalence of T1D among children aged 0–18 years living in Samsun, the largest city in Black Sea region of Turkey.

Methods: Medical records of Pediatric Endocrinology Units at University and State Hospitals in Samsun provided the primary source of ascertainment. The secondary independent data source was based on the list of children on insulin treatment reported by the schools upon our request. By visiting the schools, children on insulin treatment were confirmed and classified as T1D or other types of diabetes. Patients with secondary, type 2 and chemotherapy-induced diabetes were excluded.

Results: We identified a total of 192 children with T1D, including 31 new onsets, among 364 218 children aged 0–18 years during a period between May 1, 2011 and April 30, 2012. The overall prevalence and incidence rates for T1D were 0.53/1000 (95% confidence interval [CI] 0.52–0.54) and 8.5/100 000 (%95 CI 8.2–8.8) per year, respectively. The rates according to age groups are shown in Table 1.

Conclusions: The prevalence (0.66/1000) for school age (6–18-year-old) children in our cohort is in great agreement with the result (0.67/1000) of very recent study conducted in 1.6 million children in Istanbul, Turkey. Although the annual incidence (8.5/100 000) of T1D in our pediatric population is slightly lower than the mean rates (between 10–20/100 000) of many European countries, it is considerably higher than those (<3/100 000 in general) of Asian countries. These frequency rates suggest that people living in Turkey located at the intersection of Asia and Europe may have a relatively moderate risk for development for T1D.

Table 1. Prevalence and incidence according to age groups.

Age groups (years)	Number of population	Number of children with new onset T1D	Total number of children with T1D	Incidence per 100 000 children (%95 CI)	Prevalence per 1000 children (%95 CI)
0–5	88 964	3	9	3.4 (3.0–3.8)	0.10 (0.09–0.11)
6–11	117 126	11	59	9.4 (8.8–10.0)	0.50 (0.49–0.51)
12–18	158 128	17	124	10.8 (10.3–11.3)	0.78 (0.77–0.79)
6–18	275 254	28	183	10.2 (9.8–10.6)	0.66 (0.65–0.67)
0–18	364 218	31	192	8.5 (8.2–8.8)	0.53 (0.52–0.54)

P-399-170

Increased incidence and severity of diabetic ketoacidosis among newly diagnosed type 1 diabetes mellitus in children of West Texas and Eastern New Mexico

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Background: Children with new-onset diabetes can present in diabetic ketoacidosis (DKA) if the diagnosis is delayed. DKA carries high morbidity and mortality rate and can be prevented by recognition of early symptoms of diabetes.

Objectives: To determine the incidence and severity of DKA and to identify risk factors leading to delay in seeking medical care for new-onset Type 1 diabetes mellitus (T1DM) for Lubbock county and surrounding areas with very low population density.

Design and methods: Retrospective chart review of all patients <18 years who presented with new-onset T1DM from January 2007 to December 2010 and were followed by Texas tech university health sciences center (TTUHSC) endocrinology department. DKA was defined as serum glucose >200 mg/dl, bicarbonate <15 mmol/l and presence of serum or urine ketones.

Results: Overall, 124 subjects presented with new-onset T1DM, and 117 had laboratory testing done upon the presentation. Forty eight of them (41%) presented with DKA, and 14 children (11%) with severe DKA (HCO3 <5 mmol/l). 23 children were younger than 6 years and 11 children younger than 4 years age. In the youngest population (<4 years), 100% presented in DKA and 45% (6) in moderate to severe DKA. In our study population, a greater percentage of children (38%) presented in DKA with new-onset T1DM compared to national and international data (15%–25%). Only age was statistically significant risk factor, with younger children having more severe presentation at the time of diagnosis. When severity of DKA was correlated with the insurance status, distance to the referral hospital, HbA1c and duration of self-reported symptoms of diabetes, we found no significant differences.
Conclusions: Presentation in severe DKA commonly indicates a delay in seeking medical care due to delayed recognition of the symptoms of T1DM. A high index of suspicion on the part of parents and health care providers may reduce morbidity and cost of initial health care.

P-351-171

Decline of C-peptide during the first year after diagnosis of type 1 diabetes in children and adolescents

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One part of the explanation why immune interventions fail in several clinical trials, can be that patients with type 1 diabetes, irrespective of age, sex, ethnic origin, geographical area are lumped together into one group regarded to be homogenous. However our knowledge is still limited on the natural course of residual beta cell function. In Sweden all newly-diagnosed diabetic children are included in a national study to better classify their diabetes.
Aim: We decided to study the loss of C-peptide during the first year, and how this natural course was related to different clinical factors.
Patients: 3824/4017 newly-diagnosed patients (95%) were classified as type 1 diabetes. In a non-selected subgroup of 1669 patients we also determined spontaneous non-fasting C-peptide after ca 1 year.
Results: The younger the child, the more rapid loss of C-peptide ($P < 0.001$), and the higher the C-peptide at diagnosis the larger difference when comparing with C-peptide 1 year later ($P < 0.0000$). Patients with higher BMI had higher C-peptide at diagnosis but lost a larger proportion during the first year ($P < 0.01$). Patients without clinical symptoms and signs, which is associated with higher BMI and higher C-peptide at diagnosis, also lost a larger proportion of their residual insulin secretion than patients with such symptoms ($P < 0.001$). Patients diagnosed during autumn had higher C-peptide at diagnosis, but than lost a larger proportion of their C-peptide during the coming year ($P < 0.001$). Occurrence of auto-antibodies showed no association with C-peptide course during the first year.
Conclusion: Not even in a restricted geographical area and <18 years of age, we can regard the course of type 1 diabetes as homogenous, but we should be aware of such factors as age at diagnosis, BMI, severity of symptoms and perhaps type of auto-antibodies when we compare groups of patients eg in immune intervention trials.

P-232-172

Increased incidence of type 1 diabetes mellitus in Japanese children and adolescents is less obvious than in European populations

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Objective: There were no reports of the incidence in Japanese type 1 diabetes mellitus (T1DM) children after 1990s onwards. EURODIAB report showed that the incidence of European T1DM children increased in the period 1989–2003. Our aim is to clarify the recent trend of the incidence in Japanese children and adolescents with T1DM.
Research design and methods: The incidence of T1DM aged 0–14 in Yamanashi prefecture from 1986 to 2010 was evaluated retrospectively. All patients met a criterion that at least one of the autoantibodies in anti-glutamic acid decarboxylase antibody (GAD Ab), islet antigen 2 antibody (IA2 Ab), and insulin autoantibody (IAA) were positive. We divided three groups by the aged 0–4, 5–9, and 10–14.
Results: In the whole study period (25 years), 78 new T1DM cases (32 boys, 46 girls) were registered in Yamanashi prefecture. The annual incidence in all age tended to increase recently, but not significant. The annual incidence of aged 10–14 increased 2.7%, and that in male increased 3.3%. The incidences in 0–4 years and 5–9 years of age groups did not increase significantly.
Conclusions: It is well known that the incidence of type 1 diabetes in Japan is very small in the whole world. T1DM incidence of adolescent, especially in boys, in Yamanashi has gradually increased. It may suggest that the incidence of adolescent T1DM have also increased in Japan, although the increase is less remarkable than those found in Caucasian populations.

P-149-173

Differences in metabolic control at diagnosis between sporadic and familial cases of T1D in Sweden

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Objectives: The clinical impression that there is a difference in metabolic control between sporadic and familial T1D cases was explored.
Methods: Data on 2060 males and 1644 females, 1–18 years old from the Swedish pediatric quality registry, SWEDIABKIDS, year 2007–2010 were analyzed. Of these 653 (17.6%) had first degree relatives, grandparents included, with T1D.
Results: In sporadic cases 18% of the children had pH <7.3 at diagnosis. Corresponding figures were 11% when the mother and 7% when the father had T1D. Only 5% of the children had pH <7.3 when a sibling had diabetes ($P < 0.001$). The mean HbA1c at diagnosis in sporadic cases was 95 mmol/mol. When the mother or the father had diabetes mean HbA1c was 81 mmol/mol ($P < 0.001$). The mean HbA1c was significantly lower also in children with a sibling with T1D, 76 mmol/mol, ($P < 0.001$). Even in families where a grandparent had diabetes

mean HbA1c was lower, 86 mmol/mol, (P < 0.001). In total, 7% of the children with a relative with T1D had pH <7.3 (P < 0.001) and a mean HbA1c of 79 mmol/mol compared with sporadic cases (P < 0.001). No difference was found in age at onset, duration, blood pressure, insulin dose or BMI between families with more than one family member with T1D compared to sporadic cases. No difference regarding Hba1c at clinical follow up was seen between children with a parent with diabetes compared with sporadic cases. On the other hand in families with more than one child with T1D, HbA1c in the children was significantly higher than in families with sporadic cases 62.0 and 57.9 mmol/mol, respectively (P < 0.01).
Conclusions: The less severe clinical manifestations at onset in the second affected family member may result from increased awareness of T1D. Families with more than one child with T1D need extra support from the pediatric diabetes team to reach and maintain a good metabolic control.

P-2-174
Glucose tolerance, insulin secretion and sensitivity in Indian children and adolescents with cystic fibrosis

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Objectives: (i) To estimate prevalence of abnormal glucose tolerance, undernutrition, and delayed puberty; and
(ii) To study insulin secretion and sensitivity in children/ adolescents with cystic fibrosis (CF).
Methods: Thirty CF patients aged 6–18 years were enrolled. Exclusion criteria were acute exacerbation/ systemic steroid use in last 2 weeks. Height, weight and pubertal stage were assessed. Fasting venous sample was drawn for glucose (BG), insulin, insulin-like growth factor (IGF)1, IGF binding protein (BP)1 and IGFBP3. Oral glucose (1.75 gm/kg) was administered and sampling done at 30, 60, 90 and 120 minutes for glucose and insulin. Patients were classified as having normal glucose tolerance (NGT) if fasting BG <126 mg/dl and 2 hours BG < 140 mg/dl, impaired glucose tolerance (IGT), if fasting BG <126 mg/dl and 2 hours BG 140–200 mg/dl, or CF related diabetes (CFRD), if 2 hours BG >200 mg/dl. Insulin secretion was assessed by first-phase insulin response (FPIR) and integrated insulin secretion (IIS), and insulin sensitivity index (ISI) by OGTT and HOMA models.
Results: Mean age was 11.2 ± 4.1 years. Abnormal glucose tolerance was present in 21.4% (95% CI: 8–40%, IGT in 5, CFRD in 1). Stunting (HAZ <-2) and undernutrition (BMIZ <-2) were present in 12 (41%) and 14 (48%). Puberty was delayed in 8 out of 10 subjects >13 years. HAZ showed positive correlation with IGFBP3 (r = 0.50, P = 0.05), whereas BMIZ was inversely correlated with IGFBP1 (r = -0.46, P = 0.01). IGF1 showed direct correlation with BMI (r = 0.36, P = 0.05).Insulin secretion was similar in subjects with IGT/CFRD (n = 6), and NGT (n = 24). IGT/ CFRD group had lower ISI (OGTT) (0.11(0.08–0.15) vs 0.15(0.11–0.17), P = 0.006) and higher ISI (HOMA) (indicating insulin resistance, 1.94 (0.64–2.11) vs 0.99(0.32–5.29), P = 0.05) than NGT group.
Conclusion: IGT (caused predominantly by insulin resistance, rather than insulinopenia), stunting, undernutrition and delayed puberty are common in Indian children with CF.

P-251-175
Diabetes mellitus among children and adolescents at Siriraj Hospital etiologies, clinical characteristics, glycemic control, and complications

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Objectives: The objectives of this study were
(i) to determine the etiology of diabetes in Thai youths,
(ii) to compare physical characteristics, clinical presentation, glycemic control, and treatment outcomes between T1D and T2D patients.
Methods: A retrospective chart review was performed in 137 patients who were newly diagnosed with diabetes mellitus during 2005–2010 at the Department of Pediatrics, Siriraj Hospital.
Results: Type 1 diabetes comprised 65.7%, type 2 diabetes 21.9%, drug-induced DM 5.8%, DM other type 5.9%, double diabetes 0.7%. Diabetic ketoacidosis was the most common clinical presentations in T1D (51.1%), followed by hyperglycemic ketosis (32.2%). T2D patients usually presented with classic symptoms: polyuria, polydipsia, and weight loss (46.7%). Age of onset (9.5 ± 3.7 years vs 12.6 ± 1.8 years, P < 0.001), BMI (17.2 ± 3.4 kg/m^2 vs 29.7 ± 7.2 kg/m^2, P < 0.001), % of patients in puberty (52.2% vs 96.7%, P < 0.001), blood glucose (488 ± 201 mg/dl vs 313 ± 134 mg/dl, P < 0.001) were significantly different between T1D and T2D patients. GAD65 and IA2 antibodies were positive in 50% and 58% of T1D patients, neither were present in T2D patients. In T1D patients, only 14.7% had HbA1c levels within recommended range for age whereas 66.7% of T2D patients had HbA1c levels within recommended range at the 3rd year of treatment. Seventy-seven percent of T2DM patients had lipid disorders in which low HDL level was the most common lipid disorders. Seventeen percent of T1D patients had high LDL level. During the 7- year F/U, 7.8% of T1D and 13.3% of T2D patients developed microalbuminuria and 3.3% of T2D patients had diabetic retinopathy.
Conclusion: Although, no increase in number of new onset T1D and T2D patients were found in this study, more numbers of patients with drug-induced diabetes and other types diabetes were recognized. Only small numbers of T1D patients achieved good glycemic control.

P-165-176
Change in the clinical picture of type 1 diabetes in children over the years 2000–2010 in Polish Podlasie Province

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Purpose: The positive influence of continuous subcutaneous insulin infusion (CSII) on metabolic control in short term studies is already proved, but the possible influence of this method on the microangiopathy and cardiovascular risk factors remains unknown. The aim of the study was to compare the clinical picture of type 1 diabetes in children over the years 2000–2010, taking into account the impact of last decade change in insulin treatment regimens.
Patients and methods: We compared 251 diabetic children, diabetes outpatient clinic patients in 2000, with 316 children treated in 2010 in Podlasie Province, Poland. Patients data were

obtained on the basis of outpatient clinic and hospital records. Demographic data, treatment regimen, type of insulin, metabolic control, the incidence of microangiopathy, risk factors of cardiovascular disease and comorbid autoimmune diseases were compared.

Results: We found a reduction of median age of diagnosis from 10 to 8 years, P = 0.03. Significantly increased the percentage of children treated with CSII (to 60.1%) and decreased the percentage of children using conventional insulins to insulin analogues. Metabolic control deteriorated, as evidenced by the increase in glycosylated hemoglobin from 7.4% to 8.0%, P = 0.02 and an increase in prevalence of patients with HbA1c >7.5% in 2010. The percentage of children with obesity increased from 5.2% to 13.7%, P = 0.004. In 2010 we noticed increased percentage of children with other autoimmune diseases: celiac disease (from 0.4% to 7.3%, P < 0.001) and thyroid diseases (from 6.9% to 21.3%, P < 0.001). Incidence of retinopathy decreased from 6% to 1%, P = 0.04.

Conclusions: Over the last decade, a significant change in the method of treatment in children with type 1 diabetes has occurred. The unfavourable deterioration of metabolic control, despite the frequent CSII use, may be due to increased prevalence of obesity and additional autoimmune diseases in today's patients.

Poster Tour 3 - Diabetes and Epidemiology

P-114-014

Type 1 diabetes mellitus diagnosis and viral diseases: an epidemiological approach

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Objectives: Both animal and human studies have provided some evidence that the initiation of type 1 diabetes mellitus (T1DM) may be triggered by viral infections. In a wide survey we aimed to evaluate a possible association between childhood viral infections and T1DM diagnosis in Greece, as well as to explore whether clinical onset of T1DM is more prevalent during months of increased morbidity in children.

Methods: Data provided by the National Statistical Service of Greece concerning new cases of T1DM were reviewed, as well as cases of infectious diseases that required hospital admission, between 1986 and 1997. The records of 811 children with T1DM (437 boys and 374 girls), aged 8.5 ± 4.5 years, were reviewed.

Results: A positive linear association was observed between new cases of T1DM and total hospital admissions due to viral infections ($R^2 = 0.720$, $P < 0.0005$). The association was also statistically significant when respiratory tract infections ($R^2 = 0.630$, $P < 0.001$) and gastroenteral infections ($R^2 = 0.748$, $P < 0.005$) were examined separately. The number of children diagnosed with T1DM during autumn and winter was significantly higher, compared with those diagnosed during spring and summer (456 vs 355 of new cases of T1DM respectively, $P < 0.0005$). The same trend was observed for both boys and girls.

Conclusions: The results indicate that the onset of T1DM may be linked to infectious diseases that may result in b-pancreatic cell damage, leading to the development of T1DM.

P-176-015

Hospitalisation among diabetic children: data from the French population-based study Entred-Enfant 2007–2010

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Objectives: To describe hospitalisations of the diabetic children (age <18 years) at the national level in France, excluding admissions at new-onset.

Methods: In 2007, a random sample of 924 children (<18 years) was drawn from the French medical insurance system among people reimbursed for oral hypoglycaemic agents (OHA) or insulin at least three times over 08/2006–07/2007. For all children, medical reimbursements and hospitalisation data from August 2007 to July 2008 were extracted. Children treated by OHA only were excluded. An algorithm based on ICD-10-coded diagnoses was used to categorise admissions: control and education, acute diabetes complications, other causes.

Results: A total of 884 children (50% boys, mean age 12 ± 4 years) were included. During the year, 52% of the children were hospitalised at least once (day care: 26%; overnight care: 35%) with a total number of 834 stays. The mean duration of stays was 1.8 days. The average cumulative duration over 1 year per hospitalised child was 3.9 days and increased with age (2.7 < 10 years and 4.4 ≥ 10 years; $P < 0.01$). The causes of hospitalisation varied with age: 34% of the 884 children (41% <5 years; 36% [5–9]; 39% [10–14] and 26% ≥15 years) were admitted at least once for ''control and education'', 12% (14% <5 years; 10% [5–9]; 15% [10–14] and 10% ≥15 years) for acute diabetes complications and 3% for micro-vascular complications. Compared to those who were not hospitalised, children hospitalised benefited more often from health insurance coverage for low-income people ($P < 0.02$), were more often followed by an hospital practitioner ($P < 0.001$) and treated by insulin pump ($P < 0.001$).

Conclusions: Hospitalisations are frequent in children with diabetes. Causes of hospitalisations vary with age but are mostly linked to control and education. The results suggest however that the ISPAD 2009 recommendation to organize an annual review of care is only partly followed in France.

P-216-016

Presence of cardiovascular risk factors in a type 1 diabetes pediatric population

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Introduction: Individuals with type 1 diabetes mellitus (T1DM) have a tenfold excess risk of cardiovascular disease (CVD) compared with that for the general population. Known risk factors for vascular complications are longstanding diabetes, age, poor glycemic control, smoking, hypertension, obesity, albuminuria and dyslipidemia. Adequate glycemic control was able to reduce the incidence of CVD by 57% in T1DM. In a German study, 69% of theT1DM pediatric patients were found to have one or more cardiovascular (CV) risk factors.

Objective: To evaluate CV risk factors in T1DM population enrolled in our service.

Methods: We analyzed 191 patients, under 18 years-old, with T1DM, through a cross-sectional study from a questionnaire, along with single anthropometric measures and laboratory work-up.

Results: The study sample consists of 65% of female patients, mean age 10.9 years, 54% of the population >11 years. Of the patients, 22% were overweight and 15% obese, with 47% of the patients below 6 years with a BMI above P > 85. The lipid profile showed decreased HDL (<45 mg/dl) in 51% (mean 49.9), elevated LDL (>100 mg/dl) in 45% (mean 100.4 mg/dl) and elevated triglycerides (>100 mg/dl) in 18% (mean 78.5 mg/dl). Blood pressure was above the target in 24%, with elevated systolic and diastolic blood pressures in 10% and 19%, respectively. HbA1c was less than 7.5% in only 14% of the patients, and up to 9% in 55%. Among the other factors were found: waist circumference above 90th percentile in 14% (21/149), being inversely proportional to age; smoking in 2%; 39% without physical activity practice and familial history of early CVD (one relative in first degree) in 28%.

Conclusion: In a population with a poor glycemic control, the recognition of high prevalence of CV risk factors, despite being an isolated measure, it should alert us to a better approach in preventing these factors in T1DM patients from childhood, and reinforce the need for improvement of glycemic control.

P-238-017

An increase in the incidence of type 1 diabetes in children aged less than 15 years in Croatia is still continuing in the period from 2004 to 2009

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Introduction: The incidence of type 1 diabetes mellitus (DM1) among children and adolescents increased markedly during the last 50 years. From 1995–2003 the incidence of DM1 in Croatian children was 8.87/100 000/person-years, which placed Croatia among countries with moderate risk for DM1. Objectives to determine incidence rates of DM1, their differences and trends among children and adolescents in Croatia from 2004–2009 and to compare the results with previous studies in Croatia and other European countries.

Methods: DM1 crude incidence rates were estimated as a number of newly diagnosed patients per 100 000/persons-year for children aged 0–14 years and three age subgroups: 0–4, 5–9 and 10–14. Standardized incidence was calculated using the method of direct standardization to WHO standard world population aged 0–14 years. The incidence rates by gender, age and calendar year, and their interactions were analysed using Poisson regression model.

Results: From 2004–2009 there were 665 children aged 0–14 years with DM1 (364 girls/319 boys). The standardized incidence was 15.71 (95% CI 9.51–21.91) per 100 000/person-year. No significant difference in incidence or incidence trend was found between boys and girls. The annual increase in incidence was 5.44% (95%CI 0.84–10.24) and was statistically significant ($P < 0.02$). Comparing age-groups, the increase in incidence was significant only in the group of 5–9 years [11.17% (95%CI 3.17–19.79); $P < 0.005$]. The increase of 4.72% (95% CI -2.28 to 12.22) in the group of 10–14 years and the negative trend of -1.78% (95% CI -10.56 to 7.83) in the group of 0–4 years were not statistically significant.

Conclusion: The incidence of DM1 in children and adolescents in Croatia is 15.71 per 100 000/person-year and is still increasing, which places Croatia among countries with high risk for DM1. Average annual incidence raise of 5.44% was markedly lower than in previous study (9.0%), but is still higher than European average (3.9%).

P-101-018

East Africans in Sweden have a high risk for diabetes type 1

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Objective: To investigate the prevalence of diabetes type 1 in children with an origin in Sub-Saharan Africa in Sweden.

Research design and methods: Nationwide register study based on retrieved prescriptions of insulin during 2009 in children 0–18 years. The study population consisted of 35 756 children in families with an origin in Sub-Saharan Africa and 1 666 051 children with native Swedish parents.

Results: Diabetes type 1 was more common in Swedish-born children in families originating in East Africa compared with offspring of native Swedish parents, OR 1.29 (95 CI 1.02–1.63), after adjustment for age and sex, and less common in children who themselves were born in East Africa; OR 0.50 (0.34–0.73). Offspring of parents from other parts of Sub-Saharan African had a comparatively low risk for diabetes type 1.

Conclusions: This study indicates that populations with an origin in East Africa have a high risk for diabetes type 1 when raised in a high income society like Sweden.

P-134-019

Important raise in the incidence of type 1 diabetes mellitus in Romanian children aged 0-14 years. The Romanian Childhood Diabetes Register

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Objectives: The purpose of this paper was to analyze some aspects regarding the incidence of type 1 diabetes mellitus (T1DM) in Romanian children aged 0–14 years, between years 1996 and 2011.

Methods: Data regarding the epidemiology of T1DM were obtained from the Romanian Childhood Diabetes Register, developed and updated every year by ONROCAD, and demographic data from the National Institute of Statistics. The incidence was calculated per 100 000 population at risk.

Results: The yearly incidence of T1DM showed an important increase over the studied interval (figure). The incidence was with 130% higher in 2011 as compared to 1996 (mean yearly increase 8.66%). The increase in incidence was present in all age groups (from 2.28 to 7.54/100 000 in group 0–4 years, from 4.05 to 10.56/100 000 in group 5–9 years and from 6.24 to 12.02/100 000 in group 10–14 years). The mean incidence was similar in boys and girls (6.77 ± 1.8/100 000 vs 6.7 ± 1.58/100 000, P = NS). There was a great variability of the mean incidence in the 41 districts (from 3.47 to 11.65/100 000). Analysis on historic regions showed that mean incidence was higher in Transilvania (7.12/100 000) than in Muntenia (5.37/100 000) and Moldova (5.67/100 000) ($P < 0.0001$).

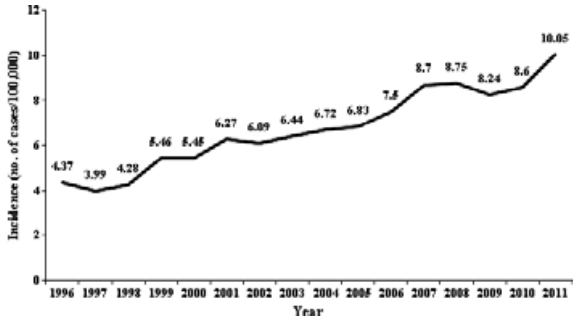

Figure: Incidence of T1DM in Romanian children (1996–2011)

Conclusions: The incidence of T1DM in Romanian children (0–14 years) showed an important increase over a 16 years interval, in all age groups. Boys and girls have similar incidence. There are important regional differences.

P-240-020

Basal C-peptide levels related to diabetes duration, HbA1c and insulin dose in children with type 1 diabetes from Romania

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Objectives: Our main aim was to establish the relation between basal C peptide, on one hand, and diabetes duration, HbA1c and dose of insulin, on the other hand.
Methods: We enrolled 426 children with type 1 Diabetes Mellitus, aged 1–17 years. Basal C peptide and HbA1c levels were measured by chemiluminiscence method (reference values: 1.1–4.4 ng/ml) first, and by immunoturbidimetric assay (reference: 4.5–5.7%) the second. The correlation was tested using Spearman's method.
Results: Main results are described in Table 1.

C Peptide levels (ng/ml)	0–0.3	0.31–0.5	0.51–1	1.1–2	2.1–4.4	P (ANOVA)
Perecentage	60.8%	12.91%	16.43%	8.69%	1.17%	-
Diabetes duration (year ± SD)	4.26 ± 3.36	1.38 ± 1.78	0.9 ± 1.29	0.96 ± 0.93	0.88 ± 0.51	<0.0001
HbA1c (% ± SD)	8.81 ± 1.82	8.47 ± 1.67	8.14 ± 1.92	7.83 ± 2.26	6.44 ± 0.36	0.0004
Daily insulin dose (UI/kg ± SD)	0.82 ± 0.25	0.64 ± 0.28	0.53 ± 0.28	0.5 ± 0.27	0.53 ± 0.3	<0.0001

We found a significant, negative, power-type correlation between diabetes duration and C peptide levels (Spearman r = -0.61, CI: -0.67 to -0.54, P < 0.001). Between C peptide levels and HbA1c we found a weak but statistical significant negative linear correlation (Spearman r = -0.24, CI: -0.33 to -0.14, P < 0.001) and between C peptide and daily dose of insulin a moderate negative correlation (Spearman r = -0.46, CI: -0.53 to -0.38, P < 0.001).
Conclusions: Almost 40% of children with type 1 DM had C-peptide level over 0.3 ng/ml. The value of C peptide is reverse correlated with diabetes duration and daily dose of insulin. A significantly improvement in glycemic control was found in children with higher C peptide values compared to ones with lower values.

P-346-021

Characteristics of patients with type 1 diabetes at diagnosis: an evolving view of the past 35 years

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Objectives: To evaluate the profile of patients with type 1 diabetes mellitus (T1DM) at diagnosis, comparing height, weight, puberty and diabetic ketoacidosis (DKA) between two periods in the last 35 years.
Materials and methods: Analysis of 382 charts of patients with T1DM, followed at the Pediatric Endocrinology Unit of Santa Casa of São Paulo Faculty of Medicine. They were divided in two groups, regarding the time of diagnosis. Group 1: born from 1976 to 1989 and Group 2, from 1990 to 2011. From this cohort, 280 were included, fulfilling the following criteria: chronological age (CA), height, weight, pubertal stage and presence of DKA at diagnosis. We considered data from the first medical visit, which had occured in an interval less than 6 months after the diagnosis. Patients with chronic disease or endocrine disease that could interfere with growth, were excluded. We calculated standard desviation scores for height (zH), body mass index (zBMI), according to data from NCHS 2000. The pubertal stage was defined according to Tanner's criteria. Statistical analysis: SIGMA-STAT 3.5.
Results: Group 1 (n = 138): CA = 8.9 years (3.4), zH = 0.23 (1.1), zBMI = -0.79 (1.3), 85 were prepubertal, 82/136 had DKA at diagnosis. Nutritional assessment: malnutrition 25%, 66.2% eutrophic, 6.6% overweight and obese 2.2%. Group 2 (n = 142): CA = 6.3 years (3.8), zH = 0.28 (1), zBMI = 0.03 (1.2), 109 were prepubertal, 97/138 had DKA at diagnosis. Nutritional assessment: malnutrition 2%, 71% eutrophic, 19.7% overweight and 7.7% obese. Statistical difference on age and BMI between the two groups (P = 0.001).
Conclusion: We concluded that the group of patients diagnosed in the last period, had this presentation at an earlier age and higher BMI. There was no significant difference on height between groups.

P-379-022

Prevalence of type 1 diabetes mellitus in 6–18 year-old school children living in Diyarbakır at the Southeast Anatolian region of Turkey

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Objective: Type 1 diabetes mellitus is the most commonly encountered chronic disease of the childhood. Its incidence rate is increasing worldwide. Prevalence rate differs according to factors like geographical location, ethnicity, gender and age. There are a few numbers of studies conducting T1DM prevalence at the childhood in our country and region. Aim of present study is to define T1DM prevalence children between ages of 6–18 years in Diyarbakir, which is one of the largest cities of the Southeast Anatolian region.
Method: Number of children with the diagnosis of T1DM at the schools were defined in cooperation with Diyarbakir Directorate of Education. Prevalence of T1DM was calculated with the obtained data.
Results: Number of patients with the diagnosis of T1DM children in school children (6–18 year-old) in Diyarbakir was 174; the prevalence of T1DM was $0.42/10^3$. Of patients, 92 (52.9%) were female and 82 (47.1%) were male; female/male ratio was 1.1/1. Prevalence rate calculated in females ($0.47/10^3$) was higher than that of males ($0.38/10^3$) (P < 0.05). Prevalence of T1DM in the centrum of Diyarbakir ($0.46/10^3$) was higher than those calculated in the districts ($0.35/10^3$) (P < 0.05). In the centrum of Diyarbakir, T1DM prevalence rate in private schools (1.26/1000) was higher than that of in government schools ($0.40/10^3$). There were no correlation between prevalence of T1DM and development indices reported by the State Planning Organization.
Conclusion: T1DM prevalence rate was calculated as $0.42/10^3$ among school aged children between 6–18 years in Diyarbakir at the Southeastern Anatolian region of Turkey. This rate is higher than the prevalence reported from Ankara in 1993, and is lower than the prevalence reported from Istanbul in 2009. Results indicated variabilities in T1DM frequency between regions of Turkey as well as the west and the east of our country.

P-27-023

Frequency of type 2 diabetes mellitus (T2DM) among diabetic children in El Minia Governorate, Egypt

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Background: T2DM in children and adolescents is becoming an increasingly important public health concern throughout the world.
Aim: To estimate the frequency of T2DM among diabetic children in El-Minia Governorate, and correlate its presence with different parameters.
Subjects and methods: 210 diabetic patients in Minia governorate were included and subjected to thorough history taking,complete examination and laboratory investigations.
Results: T2DM was presented in 13.3%, it was significantly presented in females (64.3%) and 71.4% had positive family history of DM.T2DM patients had significantly higher BMI and waist circumference centiles for age and sex than those with T1DM. Also, HbA1c%, serum C-peptide and cholesterol levels were significantly higher inT2DM thanT1DM patients. Finally, there were weak significant positive correlations between C-peptide level and both BMI and waist circumference and there was fair significant positive correlation between BMI and waist circumference.
Conclusion: T2DM is no longer a disease of adults but also it can occur in children and adolescent. Obesity, puberty and positive family history of DM are risk factors for T2DM.

P-486-024

Diagnosis and reclassification of diabetes in pediatric patients

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Background and objective: Overlapping clinical phenotype of diabetes has been caused challenge and misclassification at initial diagnosis. Therefore, we need to reexamine our patients with diabetes because of the increasing number of non-typical type 1 cases in recent years.
Patient and methods: Patients were selected from our diabetic clinics according to whether the presence or absence of diabetic ketoacidosis, incidental hyperglycemia, obesity, positive family history, autoantibodies, C-peptide/insulin levels at presentation and their clinical course, insulin requirements, HbA1c levels on follow-up. We reviewed 570 diabetics' case notes in more than last 15 years.
Results: A total of 59 (10%) patients met the above criteria of whom diagnosed as type 2 diabetes in 11 (2%), MODY in 15 (2.6%), proved in four with genetic test, mitochondrial diabetes in 2 (0.3%) and type 1 diabetes but non-typical in 31 (5.4%). All 31 patients were reevaluated and revised some of their diagnosis. Also they were test in terms of MODY possibility using the prediction model developed by Shields and at all. Diagnosis on admission was type 1 in 18 (58%), type 2 in 4 (12%), MODY in 2 (6%), atypical type 1 in 7 (22%). In 31 patients these initial diagnosis was revised average 3 years later as follows; 21 (67%) were reclassified as atypical type 1 and n 4 (12%) patients diagnosis was changed to type 2. According to the calculation model diagnosis of 6 (19%) of those patients changed to MODY, who had the score ≥40, and planned to genetic testing.
Conclusion: There is still no gold standard for diabetes classification in children. Even type 1 diabetes is usually seen in childhood but some of diabetic patients should be reevaluated for initial diagnosis according to their presentation features and clinical course. The prediction model identifies patients with MODY by avoiding unnecessary and expensive molecular screening.

P-7-025

Diabetes mellitus classification in children and adolescents: a systematic approach

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Objectives: (i) To classify diabetic patients diagnosed in participating centres and their distribution by sex and age.
(ii) To validate the SEARCH algorithm applicability to determine the type of diabetes based on classification criteria of ADA and ISPAD.
(iii) To describe and compare clinical presentation and course of type 1, type 2, or other types of diabetes.
Methods: Observational, multicenter, population study on newly diagnosed cases of diabetes. All patients between 6 months and 18 years diagnosed with diabetes in centers from Buenos Aires City and BA province, from 09/01/2012 to 08/31/2013 will be included. Total numbers of subjects: 300, considering an estimating frecuency of: 10% atipic (hybrid diabetes, type 2 diabetes and non classificable diabetes), a 4% absolut precision and 95% confidence. Neonatal, infancy, gesttional diabetes or secondary forms wil lbe excluded. A form for each patient will be filled with medical history, date at diagnose, clinical presentation, physical examination and routine laboratory test. Autoantibodies (AA) assay will be done to all patients at diagnose. It will be obtained IAA/PAA, GADA, IA-2A and Znt8A by the reference radioligand binding assay. C-Peptide will be measured in all patients under conditions of metabolic stability.
Method: Immunoassay by quimioluminiscence detections. C-Peptide after challenge will be done in children over 8 years old, that were not classified with previous test, or with mixed signs of autoimmunity and resistance to insulin action (hybrid). Classification: every patient diagnosed with diabetes will be measured for autoantibodies and fasting C-Peptide. According to these results, patients will be classified as Type 1 A, Type 2, Hybrid and untypeable diabetes. Patients with suspicion of monogenic forms will be sent to genetic testing. Those hybrid or untypeable patients older than 8 years that cannot be classified, will undergo a stimulated C-Peptide testing and AA 1 year after.

Poster Tour 1- Diabetes & Puberty & Genetics & Immunology

P-192-036

C-reactive protein (CRP) levels are elevated during the luteal phase in adolescents with type 1 diabetes

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Introduction: Female patients with Type 1 diabetes (T1D) often experience difficulties in metabolic control during the luteal phase. It is not known whether abnormal elevations of inflammatory markers during luteal phase occurs in T1D. CRP, when assessed by an ultrasensitive assay, is a marker of subclinical inflammatory process and related to risk of cardiovascular disease.
Aim and methods: To compare CRP levels during the follicular and luteal phase in post-menarcheal adolescents with T1D ($n = 20$) and healthy girls (C; $n = 22$), and to evaluate the relationship of this inflammatory marker with IGF-1 and HbA1c levels. CRP was measured with usELISA kit. Ovulation was determined by a Progesterone level during the luteal phase >3 ng/ml.
Results: T1D girls showed higher levels of CRP compared to C group in the follicular (2.1 ± 2.2 vs 1.7 ± 1 μg/ml, respectively, P = 0.02) and also during the luteal phase (4.8 ± 3.1 vs 1.7 ± 2.2 μg/ml, respectively, P = 0.002). A larger increase in CRP levels in luteal vs follicular phase was observed in T1D vs C (235 ± 57% vs 113 ± 24.8%, P = 0.03). Lower IGF-1 levels were observed only during the luteal phase in T1D compared to C (284.0 ± 66.4 vs 344.4 ± 39.5 ng/ml, respectively, P = 0.001). A similar proportion of ovulatory cycles were observed in T1D and C girls (50 and 31.8% respectively, P > 0.05). CRP levels during both menstrual phases did not correlate with HbA1c and IGF1 levels.
Conclusion: Elevations of CRP levels are observed in the follicular and luteal phases of the menstrual cycle, but a striking increase of this inflammatory marker, associated with low IGF1 levels occur in the luteal phase of adolescents with T1D. These detrimental changes may play a role in the high prevalence of chronic complications in women with T1D (Fondecyt 1100123).

P-285-037

Insulin resistance rises before puberty - with important implications for metabolic health: 10-year longitudinal study

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Objectives: Insulin resistance (IR) is higher in puberty, but it is not clear when it starts to rise, nor the impact of its doing so. Only longitudinal data can establish the relevant trends. We sought to establish when the 'pubertal' rise in IR begins, and to measure its impact on metabolic health.
Methods: EarlyBird Study. We followed 139 healthy boys(B), 128 girls(G) annually from 5–15 years, measuring HOMA-IR, % body fat (DEXA), fasting triglycerides, cholesterol-HDL ratio(CHR), adiponectin, systolic, diastolic BP (SBP, DBP). Pubertal onset was defined by Tanner stage 2 (TS2), and by detectable luteinising hormone (LH ≥0.2 mU/l) on two successive occasions. Linear mixed effects models were constructed for the pre-pubertal period, adjusting for age and %fat.
Results: IR fell from 5–7 years (B 0.59–0.38, G 0.81–0.48 units, both P < 0.001) then rose from 7–12 years in girls (0.48–1.56), 7–14 years in boys (0.38–1.08, both P < 0.001).
- The mean age at IR nadir was 6.76y (SD 1.04) B, 6.71y (1.20) G.
- The rise in IR began 3.8 years before TS2 in B, 3.9 years before TS2 in G, 4 years before LH first became detectable in both.
- Over the last four pre-pubertal years, up to but excluding year of onset (TS2), independently of %fat:
- IR rose by 19.7% in B (0.52–0.80 IR units), and by 12.7% in G (0.66–1.08), both P < 0.001.
- Adiponectin fell (B 13.0–11.3 μg/ml, G 13.9–12.8 μg/ml, both P < 0.001)
- CHR rose (B 2.3–2.8, G 2.6–2.9, both P < 0.001)
- Triglycerides rose (B 0.6–1.0, G 0.6–0.8 mmol/l, both P < 0.001)
- SBP rose (B 97.9–100.5, P = 0.07, G 2.6–2.9 mmHg, P = 0.11)
- DBP rose (B 61.1–64.9, P < 0.001, G 62.5–65.2 mmHg, P = 0.004).

Conclusions: This study is the first to examine trends in IR over 10 years of childhood. It changes current perceptions by demonstrating that the so-called *insulin resistance of puberty* starts well before puberty, and has important metabolic implications. The early rise in IR is consistent with the release of adrenal rather than gonadal hormones.

P-51-038

Impact of regular physical activity on exercise tolerance, blood glucose and heart rate variability in children and adolescents with T1DM

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Objectives: Aim of this study was to assess influence of regular physical activity on physical working capacity, blood glucose (BG) and heart rate variability (HRV) in children and adolescents with T1DM.
Methods: Sixty young patients (aged 9–17 years) with T1DM were divided into 2 groups (30 in each) depending on their weekly physical activity (*trained group* - regular training more than 3 hours/week; *untrained group* - irregular or no physical activity). All participants underwent simultaneous continuous ECG and glucose (CGM) monitoring. To determine exercise tolerance, standard power working capacity (PWC170) exercise test was performed. Measurement of mean BG and BG variability was performed for entire period; assessment of HRV was performed for 24-hours and during exercise test. Three autonomic tests were conducted: Valsalva maneuver, deep breathing, 30:15.
Results: There was no difference in age and diabetes duration among two groups (P > 0.05), HbA1c was insignificantly higher in the untrained group (trained vs untrained respectively: 9.0% vs 9.6%; P = 0.1). Also there was no difference in the autonomic tests (P > 0.05) between the two groups. In the trained group

exercise tolerance was higher, as expected (trained vs untrained respectively: PWC170 (W) 140.3 ± 53. 2 vs 89.3 ± 28.4 and PWC170 (W/kg) 2.3 ± 0.6 vs 1.7 ± 0.4; P < 0.05). Mean BG and BG variability was lower in the trained group (trained vs untrained respectively: BG (mmol/l) 8.3 ± 2.4 vs 10.0 ± 2.1 and BG variability (mmol/l) 2.4 ± 1.0 vs 3.0 ± 0.9; P < 0.05). SDNN and RMSSD for 24-hours was significantly higher in the trained group (trained vs untrained respectively: SDNN (ms) 180 ± 45 vs 154 ± 43 and RMSSD (ms) 67 ± 32 vs 48 ± 30; P < 0.05). HRV parameters during exercise test also was higher in the trained group (P < 0.05).

Conclusion: Regular physical activity improves exercise tolerance, HRV parameters (including exercises) and related with lower mean BG, BG variability but not HbA1c.

P-441-039

Situation driven difficulties in controlling diabetes among adolescents with type 1 diabetes

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Objectives: To conduct a national study for better understanding the main drivers and barriers for optimal treatment among adolescents with type 1 diabetes.

Methods: To form the basis for a national study, we performed an exploratory study using four focus groups to categorize different areas of difficulties/preferences in diabetes treatment and to gain an in-depth understanding of how adolescents with type 1 diabetes perceive different forms of treatment. 14 respondents with type 1 diabetes were involved; seven young women (age 14–18) and seven young men (age15–18). Semi-structured conversations led by a moderator not connected to the diabetes teams were audio recorded and the material was transcribed and categorized.

Results: The strongest reasons for not controlling blood sugar levels were mainly situation driven and caused by lack of routines and plans, friend's needs and other priorities. Other areas of difficulties and preferences were also identified. The negative feeling of being bound was very strong among the respondents but was less noticed among those who used the insulin-pump. The people they mostly discussed diabetes with were their parents. However, they really wanted to talk about diabetes with their doctor, who was the only person perceived having more knowledge than themselves.

Conclusions: Teenage life means need for more freedom and thus harder to stick to routines. Teen emancipation becomes even harder with diabetes. Adolescents with type 1 diabetes face several difficulties in controlling blood sugar levels which results in poor glycaemic control. These difficulties are often situation driven but can also be caused by deeper emotional reasons, which device is being used and lack of knowledge. In this exploratory study we have identified different areas to study more closely in a nation-wide study where we will use the method ''discrete choice experiment'' to identify which parameters outperform one another within different treatment alternatives.

P-339-040

Does puberty affect the physical and biochemical profile of children with type 1 diabetes

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Objective: To investigate the effect of puberty on physical and biochemical profile of children with Type 1 Diabetes Mellitus (T1DM) in a District General Hospital setting.

Method: A Cross-sectional study of 184 children aged 0–21 years, constituting 86 girls (46.7%) and 98 boys (53.3%), who attended Joint Diabetes clinic at our hospital during the preceding five years (from 1/1/07 to 25/5/12). The data was retrieved using a computerised Diabetes Database-'Diabeta 3'. We divided the children into three groups: pre-pubertal, pubertal and post-pubertal; and studied their Body Mass Index (BMI), HbA1c, Blood Pressure and Urinary Microalbuminuria profiles.

Results: Our results showed that BMI tends to be higher in the pubertal and post-pubertal group as compared to pre-pubertal group. BMI was below 20 in the majority of pre-pubertal children above 20 in a third of pubertal children and in the majority of post-pubertal children. HbA1c greater than 8% was found in 65.5% of pubertal and 81.5% of post-pubertal girls as compared to only 50% of pre-pubertal girls. HbA1c greater than 8% was found in 74% of pubertal and post pubertal boys as compared to 53% of pre-pubertal boys. Systolic BP was higher in the Post-pubertal group. It was more than 91st percentile in 68% of post-pubertal girls and 86% of post-pubertal boys as compared to 33.3% pre-pubertal girls and 17.6% in pre-pubertal boys. 4.89% of study group were on anti-hypertensives. They were all in post-pubertal group of which 77.8% were males. No significant increase in diastolic BP was noticed in any group. Borderline microalbuminuria tended to increase with age.

Conclusion: Puberty adversely affects the physical and biochemical profile of children with Type 1 Diabetes Mellitis, these effects could be persistent following puberty.

P-298-041

Primary amenorrhea in young woman with T1DM - case report

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Introduction: Primary amenorrhea is one of complications occurring in young women with type 1 diabetes (T1DM). There is not enough evidence of it's prevalence, pathogenesis and standards of diagnosis proceeding.

Case report: Eighteen-year-old patient with the history of T1DM since 5th year of age, treated with a continuous subcutaneous insulin infusion, with average HbA1c 7.2% during last 2 years was admitted to the Dep. of Endocrinology due to primary amenorrhea. The gonadotrophins in basic conditions and following gonadorelin (LH-RH) were within reference range but serum prolactin (PRL) was significantly increased. MRI confirmed the 7 mm pituitary tumor. The treatment with cabergoline (0.25 mg/day) led to normalization of PRL, restoration of regular cycles and decrease in tumor size. The normal level of antimüllerian hormone (AMH) indicated a sufficient ovarian reserve and let exclude a primary ovarian failure (POF). Due to decreased bone mineral density related

to hypogonadism and 25OHD$_3$ deficiency the vitamin D and calcium was initiated (2000 IU/day and 1000 mg/day, respectively). Because the PTH is below the referral range the patient requires monitoring towards parathyroid insufficiency accompanying T1D in autoimmune polyglandular syndromes.

Conclusion: In young female patients with T1D and primary amenorrhea the complex endocrine diagnosis should be proceed particularly with assessing the serum prolactin and function of pituitary-gonadal axis. The described case indicates that in T1D (similarly to general population) prolactinoma could be an independent cause of amenorrhea especially in patients with good control of diabetes.

Table: Hormone measurements, antibodies and densitometry.

Parameter	Value	Parameter	Value
PRL	129 μg/dl	Calcium	2.56 mmol/l
TSH	2.12 mU/l	Z-score L2-L4 (SD)	-2.4
FSH after LH-RH (U/l)	0':7.5; 30':19.9;60':19.1	25OHD3	6.38 ng/ml
LH after LH-RH (U/l)	0':5.6; 30':96.5;60':60.2	tTG-IgA	<5 U/ml
PTH	9.0 pg/ml	tTG-IgG	<7 U/ml
a/TPO	13.1 IU/ml	AMH	2.7 ng/ml

P-374-042

25(OH)D concentration in children with IDDM

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Objective: Vitamin D deficiency has been associated with several adverse health consequence including autoimmune diseases. Hypovitaminosis D as well as low vitamin D intake have been identified as a risk factor for the development of autoimmune diseases including IDDM. But still there is small clinical information about vitamin D status during IDDM in children.

Methods: Between October and April we measured concentration of Vit.D (25-OH)D, PTH, Ca, P, ALP and BMD (L2-L4, total and total less head) and BMI in 56 children(31 girls and 25 boys) with IDDM since 4.9 years ± 3.9 (min.1.0, max. 11.8), aged 14.8 ± 1.0 (11.4–17.8), age of beginning IDDM 9.8 ± 3.9 (2.5–17.0), metabolic control -HbA1c-7.8 ± 1.7(5.1–13.6) and correlations between this factors.

Results: In 44 IDDM children(78%) concentration 25(OH)D was <20 ng/ml (insufficiency)and in 12 (22%) <10 ng/ml (deficiency). 25(OH)D correlate negatively only with HbA1c (r = -0.38, P < 0.005) but we observed that decrease of 25 (OH)D concentration was connected with decrease of Ca concentration, decrease values of BMD(only total less head), and Z-score(only total less head), BMI and the age at the moment of diagnosis. Decrease of 25 (OH) D concentration was connected with increase concentration of PTH and P and duration of diabetes. There were no influence of sex on vitamin D concentration.

Conclusions: There is still no agree as to the meaning of vitamin D deficiency during the autoimmunological diseases including IDDM specially in children and no idea as to the necessity, form and doses of supplementation. Long term observations of intervention are necessary to assess the influence of supplementation on physiological parameters IDDM in children including metabolic control and calcium and bone metabolism.

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P-396-043

Autoimmune diseases associated with type 1 diabetes mellitus

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Introduction: Type 1 diabetes mellitus (T1DM) may be associated with autoimmune endocrine or non-endocrine diseases in poliendocrine autoimmune syndromes. The incidence of these associations varies between different studies.

Aim: To identify T1DM children which associate autoimmune thyroid disease (ATD) and/or celiac disease (CD) without clinical signs.

Method: The studied lot included 24 known T1DM children (8 M and 17 F) which, beside the diagnosis protocol for ATD (TSH, FT4, TG atb, TPO atb, thyroid echography) were also screened for CD, meaning the evaluation of the anti-endomysium and anti-tissue transglutaminase (IgA class).

Results: ATD with hypothyroidism was found in six cases (F) of which, two cases even since onset of DM and four after an evolution of DM below 5 years. In all cases substituive treatment with L-Tyroxin was initiated which lead to a better control confirmed by a 0.8% decrease of HbA1c. Celiac disease (CD) was diagnosed in two cases: one case (F) within the first year of DM evolution, which also associated ATD even since the onset of DM. The second case (without clinical signs) was diagnosed after 7 years of evolution of DM, by the determination of the antibodies and was confirmed with pathological exam (small bowell biopsy). In both cases, gluten free diet was recommended. The incidence of ATD in the studied lot was 25% while for CD it was 8%. The incidence of both disease is concordant with the reported literature data.

Conclusions: The screening for autoimmune diseases should be included in the evaluation of the child with T1DM. In the studied lot, the ATD was found only in female patients. In T1DM children with poor glycemic control, even with insulin pump therapy screening for CD is needed.

P-326-044

Autoimmune thyroiditis in a population with a low incidence of type 1 diabetes

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Republic of Macedonia is a ''cold spot'' for type 1 childhood diabetes (DT1) with an incidence of 5.3/100 000/year. It is known that thyroid autoimmunity appears in diabetic children more frequently compared to the general age matched population. There are no data on the incidence of autoimmune thyroid disease in Macedonian diabetic children.

Objective: To assess the association of DT1 with autoimmune thyroiditis in Macedonian children and adolescents diagnosed and followed during a period of 14 years.

Material and methods: Newly diagnosed patients at the age <15 years in the period 1998–2011 were drawn from the diabetes register. Assessment of the thyroid function was performed at diagnosis and yearly afterwards through measurement of TSH, T4, thyroid peroxidase (TPO) antibodies titer, and ultrasound examination.

Results: 377 children (188 males) were registered during the 14 years period. TPO positivity was detected at diagnosis in

8.2% in the total group (10.3% in females), and the prevalence of TPO positivity after 14 years of follow up was 14.2% (20.1% in females). In two children thyroiditis preceded the diabetes, and in two children it was present at the diagnosis of DT1. After 14 years of follow up overt autoimmune thyroiditis with elevated TSH, positive TPO antibodies and typical ultrasound appearance was present in 14 children (3.7%) with female to male ratio of 1.8 : 1. Age at appearance of hypothyroidism was 12.7 years average (range 8–18 years). Overt hypothyroidism appeared 4.5 years average (range 0–7 years) after the diagnosis of diabetes. All hypothyroid children receive therapy with levothyroxine.

Conclusion: The TPO positivity and hypothyroidism in diabetic children are less frequent in the Republic of Macedonia compared to other European populations. Regular check up of the thyroid function in diabetic children provides timely diagnosis and treatment of autoimmune thyroiditis.

P-181-045

Follow-up of children with type 1 diabetes and positive anti-tissue transglutaminase antibody levels in 6 Flemish pediatric diabetes centres

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Introduction: The prevalence of celiac disease (CD) in patients with type 1 diabetes (T1D) greatly exceeds the prevalence of CD in the general population. The aim of this study was (i) to assess the prevalence of CD in children with T1D in six Flemish pediatric diabetes centres, (ii) to evaluate the diagnostic and therapeutic pathways used and (iii) to develop a valid protocol for screening and treating CD in T1D.

Methods: This is a multicentre (six centres), retrospective study.

Results: A total of 997 patients with T1D were screened for CD, 60 (6%) of them had elevated anti-TTG antibodies (Abs). Within 4 years after the diagnosis of T1D, 90.5% of the seroconversions had occurred. Of the 43 patients who had undergone a duodenal biopsy, 34 (23 girls vs 11 boys (P = 0.005)) were diagnosed biopsy-proven CD (3.4% of patients with T1D). These were younger at onset of T1D than those without CD (mean 5.88 vs 7.37 years). Only 16 of 60 patients with positive Abs had complaints that might be related to CD. Fifteen had a positive biopsy, 13 reported to be on a gluthen-free-diet (GFD) and all but one felt an improvement after initiation of this diet. At 1 year follow-up, there were no anthropometric differences between patients with a positive serology who were on a strict GFD and those who weren't. Interestingly, spontaneous normalization of the anti-TTG Abs was seen in 20% of the patients, two of these 12 patients even had biopsy proven CD! The mean interval between the appearance and normalization of anti- TTG Abs was 2.23 years. These patients often had lower levers of anti-TTG Abs.

Conclusion: In agreement with earlier studies, we observed that 6% of our patients diagnosed with T1D had elevated anti-TTG Abs. This study is the second to describe the high degree of spontaneous normalization of anti-TTG Abs. Therefore, we suggest that physicians should consider serologic follow-up diet for at least 12 months in asymptomatic T1D patients with mildly increased anti-TTG antibodies.

Poster Tour 2 - Diabetes & Puberty & Genetics & Immunology

P-138-026

MicroRNAs miR-21a and miR-93 are down regulated in peripheral blood mononuclear cells (PBMCs) from patients with type 1 diabetes

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Introduction: It is well established that type 1 diabetes (T1D) is an autoimmune disease. Controversial data exists regarding the differential control of the immune system in T1D patients compared to unaffected individuals. MicroRNAs (miRNAs) are involved in the control of gene expression (by negative regulation of gene expression at post-transcriptional level, by mediating translational repression or degradation of the mRNA targets). Their potential role in T cell activation and autoimmunity is controversial.
Aim: We investigated the expression profile of miR-21a and miR-93 in PMC samples of 20 T1D patients and 20 healthy controls by means of qPCR in different glucose concentrations (basal, 11 nM and 25 mM), and we analyzed the possible relationship of this expression pattern with autoimmunity.
Results: MiR-21a was significantly underexpressed in T1D samples (media values expression 0.23 + 0.05, $P < 0.01$) compared to controls (values less than 1 indicate a decrease in gene expression). When the PMCs were incubated with glucose 11 mM and 25 mM, miR-21a expression decreased in controls and increased in T1D samples (0.506 + 0.05, $P < 0.04$). MiR-93 was underexpressed in T1D patients (0.331 + 0.05, $P < 0.02$) compared to control samples. However, when the PBMCs were incubated with glucose, no changes were observed. No association with autoimmunity was observed.
Conclusion: We demonstrated that miRNAs have a differential expression in PBMCs from T1D patients compared to controls, suggesting that these miRNAs or others could be involved in T cell regulation (Fondecyt 1100075).

P-259-027

Thyroid autoantibodies in relation to HLA and islet autoantibodies to ZnT8, IA-2, GAD and insulin in children and adolescents with newly diagnosed type 1 diabetes

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Aims: Autoimmune thyroid disease (AITD) is commonly found in patients with type 1 diabetes (T1D). The aim of this study was to investigate 1) the prevalence of autoantibodies against thyroid peroxidase(TPOAb) and human thyroglobulin (TGAb); 2) the association between TPOAb and TGAb with islet autoantibodies and HLA genotypes and haplotypes at onset of T1D in a large population-based cohort of children.
Methods: Better Diabetes Diagnosis (BDD) is a prospective study including almost all children below the age of 18 at onset of diabetes in Sweden. In 2433 children diagnosed between May 2005 and October 2009 blood samples at onset of T1D were analyzed for antibodies to arginine zinc transporter 8 (ZnT8RA), tryptophan zinc transporter 8 (ZnT8WA), glutamine zinc transporter 8 (ZnT8WA), glutamic acid decarboxylase (GADA), insulin (IAA), insulinoma-associated protein 2 (IA-2A), TPO and TG in addition to HLA DQB1 and DQA1 genotypes.
Results: At the time of T1D diagnosis, 12.3% of the patients were positive for thyroid antibodies; 60.8% girls. A positive association was found between both TPOAb and TGAb ($P < 0.001$) and GADA as well as TPOAb ($P = 0.039$) and TGAb ($P = 0.0015$) and ZnT8RWQA as one group. A positive association was discovered between TGAb and the genotype DQ2 ($P < 0.001$). In contrast the homozygocity and the haplotype of DQB1*0501 was found to be negatively associated with both TPOAb (homozygocity $P = 0.003$, haplotype $P = 0.006$) and TGAb (homozygocity $P < 0.001$, haplotype $P < 0.001$). The frequency of TGAb were also reduced with DQB1*0604 (homozygocity $P = 0.03$, haplotype $P = 0.003$) as well as the genotype DQB1*0302/0501 ($P < 0.01$) and DQB1*0302/X (X not 0201) ($P = 0.02$).
Conclusions: The frequency of thyroid autoantibodies was 12% already at the time of diagnosis. At risk are children with positive GADA and ZnT8RA and children with HLA DQB1*0201. HLA DQB1*0501, DQB1*0604, DQB1*0302/0501 and DQB1*0302/X (X not 0201) seemed to protect against TGAb.

P-249-028

$CD4^+$ T cell receptor Vβ repertoire analysis in newly diagnosed children with diabetes type 1 in comparison to children with a systemic autoimmune disease (systemic lupus erythematosus) and age-matched healthy controls

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Objectives: There are limited data on the quantitative expression of the T Cell Receptor (TCR) Vβ subpopulations in children with autoimmune diseases. The aim of the study was to compare the $CD4^+$ TCR Vβ repertoire among children with newly diagnosed Diabetes Type 1 (DT1), children with Systemic Lupus Erythematosus (SLE) and healthy age-matched controls.
Methods: The study cohort consisted of:
(a) fifteen newly diagnosed children with DT1,
(b) nine newly diagnosed children with SLE, all positive for ANA and anti-dsDNA prior to treatment and
(c) 31 healthy age-matched controls.
The $CD4^+$ T Cell Receptor Vβ repertoire was analyzed using three-color flow cytometry with the IOTest Beta Mark TCR Repertoire Kit (Beckmann Coulter, Marseille, France).
Results: Increased expression (defined as control mean value + 3 standard deviations) of several Vβ epitopes was noticed sporadically in both SLE and DT1 patients, and heterogeneity of Vβ discrepancies was observed. Statistical analysis revealed that the epitope Vβ4 was significantly increased in DT1 children ($P < 0.001$), while the Vβ16 was significantly increased in SLE patients ($P < 0.001$), in comparison to controls. Children with DT1 did not display

oligoclonality of the $CD4^+$ Vβ epitopes, while expansion of certain TCR-Vβ lymphocyte populations was noticeable in the majority of patients with SLE.
Conclusion: Impairment of the $CD4^+$ TCR Vβ repertoire was less prominent in children with DT1 than those with a systemic autoimmune disease such as SLE, but it was still different from age-matched healthy controls. The $CD4^+$ Vβ4 epitope might be involved in the immunopathophysiology of DT1, while $CD4^+$ Vβ16 one could be involved in the mechanisms of SLE patients. Prominent diversity of TCR Vβ repertoire in SLE, when compared to T1D, may reflect underlying pathophysiologic differences between systemic and organ-specific autoimmune diseases.

P-352-029
Novel complex heterozygous mutations in *GLIS3* gene cause neonatal diabetes and congenital hypothyroidism

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Objectives: Previous studies have reported that recessive mutations in *GLIS3* gene inherited from consanguineous parents lead to syndromic permanent neonatal diabetes. We report a child who was born at the 39th week of gestation age with a birth weight of 1900 g. Diabetes developed within the first week of age with the symptoms of DKA with glucose level >20 mmol/l and undetectable C-peptide level. He suffered also from congenital hypothyroidism, patent foramen ovale with left ventricle distention and polycystic kidneys. Treatment with insulin (1.05 U/kg) and L-thyroxin (37.5 mcg) was initiated.
Methods: DNA was extracted from peripheral blood cells and sequenced using fluorescent-labelled terminating dideoxynucleotides. mRNA expression analysis was performed with qPCR.
Results: The patient proved to be a carrier of two heterozygous mutations: a frameshift (P444fsdelG) and amino acid substitution (H647R) in the *GLIS3* gene. Both mutations were inherited from his clinically healthy father and mother, respectively. Bioinformatic tools (SIFT and PolyPhen2) predicted that the H647R mutation disrupts a crucial Kruppel-like zinc finger domain. Phylogenetic analysis showed that the substituted histidine residue (H647) was evolutionally conserved since the nematoda. mRNA expression analysis showed that the proband (P444fsdelG/H647R) had *GLIS3* expression level lower than 1% of those observed in healthy controls, while *GLIS3* mRNA levels in parents were more than 15 times lower than median expression in healthy controls ($P = 0.02$). Further bioinformatic analysis also revealed two evolutionary conserved binding sites for the Glis3 transcription factor within the promoter region of *GLIS3* gene suggesting an autoregulatory mechanism.
Conclusion: Compound heterozygous defects of *GLIS3* may result in neonatal diabetes with congenital hypothyroidism. In view of phylogenetic and mRNA expression data we confirm that the H647 amino-acid residue is of crucial importance for the Glis3 function.

P-462-030
Natural killer T cells (NKT) in childchood new onset type 1 diabetes

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Objectives: Type 1 diabetes is a disease of autoimmune pathogenesis in which different populations of immune cells plays an important role in the initiation and modulation of immune response against antigens of pancreatic islet β cells. NKT cells (natural killer T cells) are a heterogeneous group of cells that plays an important role in the immune response affecting the activity including dendritic cells, T cells, B cells, Tregs through several secreted cytokines. It seems that by their production of Th2 cytokines, NKT may have a protective role against autoimmune diseases, including type 1 diabetes. The aim of our study was to evaluate circulating natural killer T cells (NKT) in children with new onset type 1 diabetes and comparison to a group of healthy children.
Methods: The study group comprised 32 children, mean age 10 ± 5 years, with newly diagnosed type 1 diabetes. In all children were assessed C-peptide and anti-GAD and anti-IA2 antibodies to confirm autoimmune pathogenesis of disease and cell subpopulations were examined using flow cytometry. The reference group consisted of 20 healthy children. We analyzed the percentage of $NKT3/161^+$, $NKT/4^+$ cells.
Results: In the blood of children with type 1 diabetes the average percentage of NKT was 51.11 ± 19.60% and was significantly lower ($P < 0.05$) than in healthy children 76.56 ± 16.7%.
Conclusion: The demonstrated differences of the analyzed population of immune cells encouraging more detailed analysis of the observed dependence, because they seem to indicate certain disturbances in investigated population of cells in children with type 1 diabetes.
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P-505-031
C peptidemia and impact of clinical parameters in residual insulin secretion in type 1 diabetics

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Type 1 diabetes results from a β-cell destruction due to an autoimmune process leading to insulin deficiency. This insulin deficiency may be assessed by measuring the C-peptide which is a marker of residual endogenous insulin secretion in insulin-dependent diabetics.
Objectives: To assess the C peptidemia in young diabetics in relation to their glycemic control, and secondly to study the impact of clinical parameters on the evolution of residual insulin secretion (RIS).
Material and methods: 38 diabetics (18 boys, 20 girls), with mean age 13 ± 6 years, age of onset (AO) 8 ± 4 years and mean diabetes duration (DD) 6 ± 5 years. All patients receive a two daily injections regimen. The C-peptide levels were assayed by radioimmunoassay and the levels of glycated hemoglobin were measured by the method DCA2000. (Mean annual value: 8.3 ± 1.5% (2010), last value 7.8 ± 1.5%) (09/2012). Three groups have been considered depending on metabolic control (G1 HbA1c ≤7.5% DD: 3.6 years, G2 HbA1c >7.5% DD: 6.5 years, G3 HbA1c >7.5% DD: 6.6 years).

Results: Our results show higher C-peptide levels in G1 patients compared to G2 and G3 (Mean ± SD: 1.03 ± 0.1 ng vs 0.35 ± 0.20 ng/ml and 0.35 ± 0.09 ng/ml). In G2 and G3 the C-peptide levels are increased insignificantly (P = 0.058) from childhood to adolescence. Furthermore, C peptidemia is negatively correlated with AO (maximum values when AO is 5–11 years and decreasing in all groups with later onset). In G2, the C-peptide levels evolved from 0.44 ng/ml to 0 ng/ml after 10 years of DD respectively. RIS is correlated with insulin requirements (Insulin 1.5 UI/kg vs value of C-peptide: 0.28 ng/ml) and BMI.
Conclusion: C-peptidemia is correlated with metabolic control, insulin requirements, DD and also with AO and BMI. RIS could be promoted and maintained by some clinical parameters.

P-467-032

The influence of vitamin D3 analogue on dendritic cells subsets in childchood type 1 diabetes

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Objective: In type 1 diabetes dendritic cells (DC) plays an important role in the initiation and modulation of immune response against antigens of pancreatic islet β cells. The aim was evaluation of circulating myeloid dendritic cells (mDC) and plasmacytoid dendritic cells (pDC) in children with type 1 DM before and after application of the vitamin D3 analogue (Alfadiol) in both groups and compared to healthy children.
Methods: The study group comprised 50 children (10 ± 5 years), with new onset type 1 DM who were randomly enrolled into two groups (treated with vitamin D3 analogue or not) and subjected to annual follow-up. In all children were assessed twice the level of 25 (OH) D3, C-peptide and anti-GAD and anti-IA2 antibodies and cell subpopulations were examined using flow cytometry. The reference group consisted of 10 healthy children. We analyzed the percentage of immature myeloid DC BDCA-1^+/$CD19^-$ and plasmacytoid BDCA-2^+/$CD123^+$.
Results: In 72% of children who received Alfadiol and in 50% without Alfadiol, an increase or maintain the value of C-peptide during the annual monitoring as compared with baseline values was observed. In the blood of children with type 1 diabetes not receiving Alfadiol the average percentage of myeloid DCs was 0.79% and was significantly higher (P < 0.05) than in healthy children (0.26%). However, there were no differences in the percentage of BDCA1^+ cells between the group receiving Alfadiol and a control group. The percentage of plasmacytoid cells did not differ significantly between groups. The dynamics of changes in the percentage of DC subsets in relation to baseline (newly diagnosed diabetes) was analyzed.
Conclusion: The demonstrated differences of the analyzed parameters and the population of immune system cells encouraging more detailed analysis of the observed dependence, because they seem to indicate certain positive elements of used vitamin D3 analogue in children with type 1 DM.
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P-115-033

Vitamin D binding protein polymorphisms and risk of type 1 diabetes mellitus

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Objectives: The genetic substrate of type 1 diabetes mellitus (T1DM) is an area of extensive research and vitamin D is a potential factor under investigation. Vitamin D binding protein (DBP) is a highly polymorphic protein that has been implicated in the development of the disease. Aim of the study was to evaluate the effect of two different single nucleotide polymorphisms of DBP on susceptibility to T1DM, at 416 (Asp → Glu) and 420 (Thr → Lys) codons of exon 11 at the DBP gene.
Methods: 172 subjects were enrolled in the study, 90 patients with T1DM and 82 controls. The two groups did not differ in gender distribution. Variants at the specific loci were identified by restriction mapping, following polymerase chain reaction.
Results: Allele frequencies for the polymorphism at 416 codon were similar between the two groups (P = 0.743), while differences at 420 codon were at the borderline of significance (P = 0.076). Lys/Lys haplotype was found in 6.7% of the T1DM group, while not one subject with this haplotype was observed in the control group. Lys/Lys haplotype was found to increase the risk of T1DM by 90.5% (P < 0.05), and so did the genotype combination Asp/Asp-Lys/Lys, while the combination Asp/Asp-Thr/Lys seemed to confer some protective effect against the disease (relative risk 0.64, P < 0.05).
Conclusions: These data reinforce the association between the genetic variation at codon 420 of DBP ant T1DM; however question the association of the polymorphism at codon 416 with the disease. Lys/Lys haplotype may have the most adverse effects to T1DM susceptibility.

P-280-034

Symptomatic auto-immune gastritis in two young patients with type 1 diabetes

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Objectives: Screening of anti-H^+/K^+ ATPase autoantibodies (AABs) is not routinely recommended in youth with type 1 diabetes (T1D), but our center is currently screening a large cohort of young patients. Here we report two young patients with T1D who presented diverse symptoms of autoimmune gastritis.
Patients: Patient 1, an 11 year old boy, had diabetes at 5.5 years, with positive GAD and ZNT8 AABs, negative thyroid AABs (TSH 2.8 mU/l); he is treated with 0.8 U/kg insulin (aspart-detemir) and mean HbA1c was 7.6%. Patient 2, a 13 years old girl, had diabetes at 4.5 years, with positive GAD and IA2A AABs, positive thyroid AABs (TSH 4.3 mU/l, T4L 8.3 pmol/l). She is treated with 1.4 U/kg insulin (lispro/pump) and mean HbA1c was 7.5%. Both had negative anti-transglutaminase AABs. Following revealing symptoms, anti-H^+/K^+ATPase AABs were tested on previously collected frozen samples, along

with other bowel disease AABs: anti- Saccharomyces Cerevisiae (ASCA), anti-Neutrophile Cytoplasmic (ANCA), anti-AIE 75 (typical of autoimmune enteropathy).
Results: Patient 1 presented at local hospital emergency unit for vomiting in the last few days and epigastric pain. Abdominal echography was normal; Hb was 12.5 g per 100 ml, MGV 77fl; he was diagnosed as having gastritis. For patient 2, routine annual day care hospitalization for type 1 diabetes showed iron-deficiency anemia, in a girl with no menarche: Hb 9 g per 100 ml, VGM 64fl, plasma iron 4 mmol/l (Nl 9–30), ferritin 8 mg/l (Nl 14–197). Search for anti-H^+/K^+ ATPase AABs on previously collected serum samples were positive in both patients: 39 IU/ml in patient 1, >100 IU/ml in patient 2 (Nl <15). Other AABs (ASCA, ANCA, AIE 75) were negative. Gastro-duodenal fibroscopy is planned to confirm the diagnosis. Anti-H^+/K^+ ATPase AABs have been found in 6.1% of 313 patients with T1D (3.8% in boys, 8.5% in girls).
Conclusion: Auto-immune gastritis may have diverse clinical expression, such as epigastric pain and iron-deficiency anemia, in youth with type 1 diabetes.

P-438-035

Plasma insulin glargine and its metabolite M1 and M2 after subcutaneous injection of therapeutic doses in young children with T1D: results from the PRESCHOOL study

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Objectives: In vivo, after subcutaneous (sc) injection, insulin glargine (GLA) is enzymatically processed into metabolites M1 and M2. In vitro, GLA exhibits higher, while M1 and M2 exhibit lower, mitogenic properties and affinity for IGF-1R versus human insulin (HI). In adults with T1D or T2D, the principal circulating active GLA component is M1. This study aimed to quantify plasma concentrations of GLA, M1, and M2 after sc injection of GLA in young children with T1D.
Methods: Children with T1D aged 1–6 years from the PRESCHOOL study ($n = 61$) were treated with GLA for 24 weeks and had blood samples drawn ≥24 hours after last dose at Wks 1, 2, and 4. C_{trough} plasma levels were determined using immunoaffinity purification and LC-MS/MS. Lower limit of quantification (LLOQ) was 0.2 ng/ml.
Results: M1 was the principal active circulating GLA component in plasma. Mean ± SD plasma M1 C_{trough} values were 0.580 ± 0.786, 0.458 ± 0.700, and 0.452 ± 0.583 ng/ml at weeks 1, 2, and 4, respectively. Mean GLA and M2 concentrations were below the LLOQ, indicating no GLA or M2 accumulation. Similar results have been observed in adults.
Conclusions: For young children with T1D, the principal circulating active GLA component is M1, which is no different from HI in terms of IGF-1R binding and mitogenesis. These data provide added evidence for the safety profile of GLA in young children; further studies are needed to confirm M1's lower affinity for IGF-1Rn in these patients.
This study was supported by Sanofi.
Keywords: Insulin glargine metabolism, young children
[Note to ISPAD: selected data in this abstract were previously presented at the EASD 2011 meeting in Lisbon, Portugal]

Poster Tour 3 - Diabetes & Puberty & Genetics & Immunology

P-477-056

Diabetes diagnosed in the first months of life is always a diagnostic challenge - a rare case of thiamine-responsive megaloblastic anaemia associated diabetes mellitus

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Background: When diabetes appears in the first 6 months of life it is called neonatal diabetes and is often related to a monogenic disease. The onset of a neonatal diabetes should alert to look for other symptoms in the individual and should give reason for further diagnostic investigations.
Case: We report on a 4 years old boy who was diagnosed with diabetes in his 6th week of life and is on insulin pump since then. His insulin requirements are 0.6 units/kg weight per day, the A1c 6.4%. Additionally, he has a neurosensory hearing loss that was supposed as result of a connate cytomegalovirus infection as he had a pancytopenia at the age of 6 weeks and a positive CMV antibody status. Furthermore, a macula dystrophy was diagnosed at the age of 2.5 years.
Results: The patient's karyotype is 46 XY. Wolfram's syndrome and a unilateral isodisomy of chromosome 6 were excluded. Sequencing of the KIR 6.2 (KCNJ 11), the SUR 1 (ABCC8) and the INS genes did not show any pathological results. As he also shows a muscular hypotonia a mitochondrial disease was discussed, but not found. When he was presented to our outpatient clinic the routine blood examination revealed a megaloblastic anaemia. After vitamin B12 deficiency was excluded, we thought of thiamine responsive megaloblastic anaemia (TRMA) as cause of his symptoms. The molecular testing revealed a homozygote mutation in the SCL19 A2/ TRMA-gene: c.242dupA; p (Tyr81fs*). Treatment with thiamine (100 mg/day) was started.
Conclusion: TRMA is an autosomal recessive inherited condition, characterized by a megaloblastic anaemia, non-autoimmune diabetes and neurosensory hearing loss. The extent of the symptoms could probably have been reduced if the boy had been treated earlier. This case shows the importance of thinking of TRMA if diabetes occurs in the first months of life and is accompanied by anaemia and hearing loss especially when parents are consanguine.

P-527-057

HLA-DQB1* alleles and genetic susceptibility to type-1 diabetes mellitus

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Objective: The objective was to determine HLA-DQB1 allele association with susceptibility to Type 1 Diabetes (T1D) and to the clinical and laboratory findings.
Methods: This study was conducted on 85 Egyptian children with TID and 113 age and sex matched healthy subjects. HLA-Class II- DQB1 allele typing was done using InnoLipa HLA-DQB1 update kit
Results: The frequency of HLA-DQB1 alleles *02, *03 was increased, and HLA-DQB1 *06 was decreased (Pc < 0.001) in T1D patients. The HLA-DQB1 subtypes *0201, *0202, *030201 were positively associated (Pc = 0.014, <0.001, and <0.001 respectively), and the HLA-DQB1*060101 was negatively associated (Pc < 0.001) with T1D.HLA-DQB1 genotypes 02/02, 02/03 were higher, and 03/06, 06/06 were lower in T1D patients (Pc = 0.01, <0.001, <0.001, 0.04 respectively) No relations were found between different HLA-DQB1 alleles /genotypes and grades of diabetic control, Microalbuminuria, demographic, and laboratory findings.
Conclusion: The Current work suggests that HLA-DQB1 alleles *030201, *0202, *0201, and genotypes 02/03, 02/02 may be a susceptibility risk factors for development of T1D in Egyptian children, and HLA-DQB1 *060101 allele, 03/06, 06/06 genotypes may be protective factors. HLA-DQB1 alleles and genotypes do not contribute to microalbuminuria or grades of diabetic control.

P-1-058

17q12-q21 variant is associated with early-onset type 1 diabetes

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Objective: To evaluate the relevance between type 1 diabetes susceptible SNP and the age at diagnosis by the quantitative trait locus (QTL) analysis.
Methods: We examined 428 Japanese patients with type 1A diabetes onset 16 and under, and 457 control subjects. Regarding the study design, we adopted the candidate SNP study to secure the statistical power. We selected 64 SNPs among type 1 diabetes susceptibility SNPs previously published with T1DBase and PubMed. After the SNP genotyping and the quality control checks, we performed the age-specific QTL analysis of these SNPs by Welch's t test. To address the problem of multiple comparisons, the Bonferroni correction was employed. Furthermore, to identify a cut-off age for classification into an early-onset group and a late-onset group, we performed the order-subset analysis (OSA).
Results: There is only one SNP that is regarded as significant by the genotype mode (comparison between three genotype groups) after the Bonferroni correction; *ORMDL3-GSDMB* rs2290400 is located in 17q12-q21. The OSA let us set 5 years old of cut-off age for the difference between two groups becoming maximum. Regarding the allele frequency, the risk allele frequency (RAF) of only the under 5 years onset group increases in comparison with the control subjects (38.6% vs 25.9%), and there is no difference in the RAFs between over 5 years onset group and control subjects (24.9% vs 25.9%).

Conclusions: We reveal that 17q12–q21 variant is associated with the early childhood onset of type 1 diabetes in the Japanese population. The 17q12–q21 variants were reported having susceptibility of not only type 1 diabetes but also bronchial asthma and inflammatory bowel disease by the GWAS. In particular for asthma, the younger onset, the stronger the relevance of this region, like the present study. It is unclear the participation mechanism of type 1 diabetes of 17q12–q21 variant and why an onset risk of type 1 diabetes increases only in early childhood.

P-139-059

Dysregulation in apoptosis: high expression of *xiap* gene in peripheral mononuclear cells from type 1 diabetic patients

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Introduction: Type 1 diabetes mellitus (T1D) is an autoimmune disease characterized by a progressive destruction of pancreatic β cells. It has been reported that patients with autoimmune diseases (including T1D) exhibit decreased expression of caspase 3 and others pro- apoptotic markers in peripheral blood mononuclear cells (PBMCs) and increased expression of anti- apoptotic proteins as well.
Aim: The objective of this study was to estimate the expression of apoptosis markers in PBMCs from T1D patients cultured with high glucose concentration in an attempt to mimic onset conditions. Finally we compared the expression values with clinical history, age of onset, years of disease, ketoacidosis and autoantibodies.
Results: At 11 mM of glucose the pro-apopotic gene *fas* showed a 7-fold decreased expression in the T1D group compared than controls meanwhile *bax* showed a 50-fold decreased expression (medians 0.14 and 0.02 respectively, considering patients as 1). At 44 mM of glucose there is a decreased expression of the same genes, but less abrupt (medians 0.75 and 0.47). Only the anti-apoptotic gene *xiap* showed a 2-fold increased expression at 11 mM of glucose (median 2.3). The others genes as *cas3* and *bcl-xL* did not reveal any significant expression when we compared T1D samples and controls. Regarding the clinical history no relationships were observed with age of diagnosis, ketoacidosis, glucose of debut or GAD-65 and IA-2 titles.
Conclusion: We can conclude that apoptotic mechanisms in PBMCs of T1D patients under high glucose conditions are altered and this is proved by the decreased expression of pro-apoptotic genes *fas* and *bax* and by the increased expression of anti-apoptotic gene *xiap* (Fondecyt 1100075).

P-241-060

Clinical and cytogenetical diversity of diabetes in children below two years of ages

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Objectives: Diabetes in neonatal and infancy period are usually nonautoimmune and monogenic, and ethiological factors are different than older ages. Neonatal diabetes which is seen in first 6 months of life, the mutations of genes coding Kir6.2, SUR1 and INS are the main causes of diabetes, while after 6 months autoimmunity is the main ethiological factor.
Methods: We evaluated the patients diagnosed as diabetes before 2 years of age during ten years period. On admission, clinical and laboratory charecteristics including coexisted features, autoantibodies (Anti-GAD, ICA, AIA), and molecular analysis were investigated.
Results: Nine patients who below the 2 years of ages were diagnosed as diabetes. Age of diagnosis were between 3 days and 1.7 years (9.11 ± 8.83 months). Four of them admitted to clinic with diabetic ketoacidosis. Autoimmunity were detected in five patients, and one of them diagnosed as IPEX-like syndrome because of CD25 deficiency. Five of eight patients were below 6 months of age, and five of them had monogenic form of diabetes. In two patients with neonatal diabetes K_{ATP} channel mutation were detected. Family history were positive for type 2 diabetes in four patients, and one of them also had two cousins with Wolfram syndrome (WS). All patients were began to insulin treatment. The mean doses of insulin requirement was 0.76 U/bodyweight/day. In a patient with *KCNJ11* gene mutation, succesfull transfer from insulin to sulfonylurea treatment was occured.
Conclusion: This small group showed that, diabetes in early ages have very different clinical and genetical characteristics. Although diabetes seen in these ages usually are monogenic, autoimmune diabetes are consist of considerable amount of them. Monogenic form of diabetes generally present before 6 months of ages. In patient with WS, duodenal atresia and hydrocephaly that are not reported before with WS might be related to *WFS1* gene itself or might be related to another possible gene defect.

Table: Patients Characteristics

Case	Sex	Birtweight (g)	Age of Diagnosis	DKA at presentation	Autoantibodies	Additional features	Genetical Studies	Diagnosis
1	M	3500	1.5 years	yes	yes			Type 1a DM
2	F	3750	11 months	yes	yes			Type 1a DM
3	F	3000	1,7 years	yes	yes			Type 1a DM
4	F	3100	6 months	yes	yes			Type 1a DM
5	M	3300	2 months	no	yes	Immun deficiency, enteropathy	CD25 deficiency	IPEX-Like Syndrome
6	M	2000	1 months	no	no	Epilepsy	ABCC8 gene, Exon 25, D1039N heterozigous mutation	Persitent Neonatal DM
7	M	1060	3 days	no	no		KCNJ11 gene Exon 1 E322A and D452H heterozigous mutation	Transient Neonatal DM
8	M	2960	1,7 years	yes	no	Duodenal atresia, Hidrocephaly, Primary hypothyroidism	WFS1 gene, Exon 8, V412fs homozigous mutation	Wolfram Syndrome
9	M	2600	2 months	yes	no	cleft palate	KCNJ11, ABCC8 and INS genes were normal	

[Patients Characteristics]

P-524-061

Enterovirus infection and low Treg function: two possible biomarkers of progression to autoimmune T1D

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Background and aims: Diabetes-related autoAbs, high-risk HLA-II haplotypes, and low first-phase insulin response are the main risk markers of progression to disease in siblings of T1D patients. Environmental factors may also play a critical role. T regulatory cells (Tregs) activity is commonly reduced in autoimmune disease.
Materials and methods: HLA typing, T1D-related autoAbs (IAA, GADA, IA-2A), enteroviruses (EV) in blood were determined in: one T1D patient with 14-years disease duration, his younger brother with long-standing T1D-related autoAbs, and 10 healthy controls. The two brothers shared the same high-risk HLA-II haplotypes. In all individuals the numbers and functionality of Tregs were determined. During a 3-years follow-up, the autoAb-positive brother showed a normal first-phase insulin response (90th percentile). $CD4^+$ CD25highCD127low Tregs in all subjects were evaluated by FACS, sorted, and cultured in vitro for functional analysis. RT-PCR assays targeting ≥100 EV types (5′UTR, 5′UTR-VP2, and 3D genome regions) were used for EV detection in blood.
Results: The diabetic child and his asymptomatic parents were carrying an EV of the B species in blood. The autoAb-positive brother and all healthy controls were EV-negative. Treg functionality was significantly reduced in the diabetic patient as compared to the autoAb-positive brother and the healthy controls.
Conclusions: These limited observations indicate that overt diabetes is associated with T1D-related autoAbs and, possibly, chronic EV infection. The diabetic child also showed reduced Treg functionality. Glucose homeostasis appeared to be conserved in the sibling showing T1D-related autoAbs but not carrying virus in blood. Normal Treg functionality seems associated with normal glucose homeostasis. Thus, serial determinations of EV biomarkers and Treg functions may be of value in predicting the progression to overt disease in siblings of children with T1D.

P-431-062

Type 1 diabetes and juvenile idiophatic arthritis: a case report

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T1DM is an autoimmune disease initiated by the interaction between environmental and genetic factors, that cause loss of immunologic tolerance to self antigens. T1DM is a polygenic, common, complex disease with major susceptibility lying in the Major Histocompatibility Complex (MHC) on chromosome 6 with other smaller effects seen in loci non HLA-related. Autoimmune diseases cluster within families and individuals, but the aggregation with some type of disease is quite rare. Our case report consists of a girl affected by T1DM who developed juvenile idiophatic arthritis. Born at term (birth weight 2.9 kg) from the mother's third pregnancy, she came to our observation at age 22 months old. Mother was from Philippines. Family history was negative for autoimmune diseases. She was admitted to hospital with a severe DKA, (glycemia 29 mmol/l, pH 6.9, BE -28.6) and immediately put on insulin therapy. GAD antibody titer was elevated. After 2 months she reported pain at right knee with swelling and intra-articular inflammation and limited movement. The C reactive protein and C3 complement were normal. The erythrocyte sedimentation rate was slightly elevated. Serology for antinuclear factor was positive. Juvenile rheumatoid arthtritis was diagnosed and she started non steroid anti-inflammatory agents (ibuprofene) and then methotrexate administration with remission of the disease. HLA was: DRB1 08, 15. This complex is not usually associated with DM1 and Arthrtis, in Caucasian population. Other genetic association studies, using genome-wide scanning strategy, have not been investigated yet.
Conclusion: The clinical phenotype of an unusual association of autoimmune diseases (T1DM and JIA), with an unusual HLA class II genes may suggest that our knowledge about HLA genes and autoimmunity needs to be improved in the Asian population (mother was from Philippines). Unknown genetic factors might have some role in the clinical phenotype.

P-403-063

ERBB3 associates with metabolic control after disease onset in children with type 1 diabetes

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Objectives: Genetic studies have identified more than 50 chromosomal regions that associate with type 1 diabetes (T1D). Whether the same regions also affect disease progression and metabolic control remains to be clarified. SNPs in genes with a presumed function in the β-cells are of particular interest. The aim was to investigate if specific SNPs associated with T1D could explain differences in metabolic control after disease onset in children diagnosed during childhood.
Methods: Blood samples were collected from 1074 children diagnosed with T1D before 11 years of age. DNA was extracted from whole blood on filter paper cards. Genotyping of *MHC*/rs2187668, *MHC*/rs7454108, *INS*/rs689, *PTPN22*/rs2476601, *IFIH1*/rs1990760, *ERBB3*/rs2292239 and *TNFAIP3*/rs2327832 was performed using TaqMan assays (ABI) on CFX384 real-time PCR system (BioRad). Genotypes were called using the SNPman software. The subjects were characterized for gender, age at diagnosis, diabetes duration, HbA1c, insulin dose and IDAA1c (calculated as HbA1c + 4 * insulin dose/kg/24 hours). Linear regression was used to test the association between metabolic control (HbA1c, insulin dose and IDAA1c) as dependent variables and SNP genotypes as descriptive variables.
Results: : rs2292239 was significantly associated with a lower IDAA1c ($P = 0.0067$) and a lower HbA1c ($P = 0.019$) in a recessive model corrected for gender, age at diagnosis and diabetes duration. None of the other SNPs had any effect on the metabolic control.
Conclusions: We have identified a risk SNP for T1D that associates with better metabolic control in children with childhood onset of disease. The candidate gene *ERBB3* has been shown to be down-regulated in human islets after cytokine stimulation, which indicates a functional role in the β-cells. Identification of SNPs that affect metabolic control could aid the

stratification of children with a poor prognosis already at baseline and hopefully reverse the future negative trend for these children.

P-329-064

Negativation of type 1 diabetes autoantibodies to glutamic acid decarboxylase (Anti-GAD) and insulin (IAA) in children treated with oral calcitriol

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Objectives: Experimental studies have pointed out the possibility of using vitamin D analogues in prevention and treatment in a spectrum of autoimmune diseases, including type 1 diabetes (T1D). With the recent knowledge of the possible implication of 1,25-dihydroxyvitamin D in the pathogenesis of T1D and the positive results of the administration of calcitriol in animal models in vivo we conducted a pilot clinical trial by treating high-risk children, positive in autoantibodies for T1D with oral calcitriol.

Methods: This prospective trial included 12 children (7 girls and 5 boys) aged 1.9–13 years at presentation, who were investigated as high-risk for T1D because of the already diagnosed association of celiac disease and autoimmune thyroiditis (4 girls), autoimmune thyroiditis at a very young age (<3 years: 2 girls, 2 boys), diagnosis of T1D in their siblings (2 boys), impaired glucose tolerance (IGT: 1 boy, 1 girl) between 2006 and 2012 at ''Attikon'' University Hospital, Athens, Greece. Serum levels of autoantibodies (ICA, anti-Gad, IAA, anti-IA2) and calcium metabolism (Ca, P, PTH, total 25(OH) vitamin D and Ca/Cr in 2-hour morning urine sample) were evaluated prior and at 6–12 month intervals after initiating 0.25 μg daily calcitriol p.o. for 1–3 years.

Results: In all children included persistent negativation of the anti-GAD (7 children) and IAA autoantibodies (6 children) was observed within 0.4–2 years. From the two children with IGT the boy had MODY 2 and the girl normalized her glycaemic profile.

Conclusions: Despite the small number of subjects and the absence of a control group, 0.25 μg of daily calcitriol is effective in disappearing the anti-GAD and IAA autoantibodies within 6 months. This simple, costless and safe strategy may prove quite effective in prolepsis of type 1 diabetes in the future.

P-322-065

An unusual presentation in a baby-girl with Beckwith-Wiedemann syndrome (BWS) with pancreatic and liver cysts

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Objective: A 3-month-old girl with postnatal development of BWS signs and multiple organs cysts is presented.

Material and results: The girl was born from a first complicated pregnancy of a 28-years-old mother with a birth-weight 2900 g at 35 weeks of gestation, with retarded cardiopulmonary adaptation and hypoglycaemic episodes, initially interpreted as diabetic fetopathy. Despite intravenous dextrose, she remained hypoglycaemic until the 12th postnatal day when she was diagnosed with a persistent hyperinsulinism (postprandial serum insulin 82 mIU/ml, BGL 2.1 mmol/l) and referred to us. At admission multiple pancreatic and hepatic cysts were diagnosed and verified by abdominal CT scan. At physical examination she did not display dysmorphic features suspicious for syndromic hyperinsulinism. We initiated treatment with Diazoxide (up to 21.2 mg/kg/day) and the hypoglycaemic episodes abated but BGL remained relatively low. The genetic testing for hyperinsulinism with a sequence analysis of the *ABCC8* and *KCNJ11* genes failed to detect mutations. At the age of 39 days the patient was re-admitted because of severe hypoglycemia with a hypoglycemic seizure. The clinical exam revealed a left-sided hemihyperplasia, hepatomegaly, omphalocele and iridic heterochromia. The diagnosis of BWS with an atypical postnatal presentation was suspected and 24-hours infusion of Somatostatin analog was started at increasing doses. After 10 days BGL increased to normal values and the treatment continued subcutaneously. Microsatellite analysis of markers on chromosome 11p15.5 demonstrated a loss of heterozygosity for the maternal allele. This result is consistent with a diagnosis of BWS due to paternal uniparental disomy of the differentially methylated region on chromosome 11. Methylation-specific MLPA is currently in progress to confirm this result.

Discussion: The challenges of treatment, prognosis and family counseling in patients with BWS are presented.

Poster Tour 4 - Diabetes & Puberty & Genetics & Immunology

P-12-046

Transition from insulin to glibenclamide in a one-month-old infant with neonatal diabetes mellitus caused by a new mutation in KCNJ11

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Background: There have now been several reports of the successful transition from insulin to sulfonylurea agents in patients with permanent neonatal diabetes mellitus (PNDM) caused by mutations in the KCNJ11 gene.
Case report: We report on a term female neonate weighting 2780 g (5.32 percentile, -1.62 SDS) with a new missens mutation in the KCNJ11 gene whose treatment was successful converted from insulin to glibenclamide. Blood glucose began to rise on day of life four. On day five, blood glucose measured 18 mmol/l and urine contained 1+ glucose without ketones and the patient's C-peptide concetration was 0.17 nmol/l (normal 0.298–2.35). The initial management of the patient's hyperglycemia included an infusion of regular insulin at a dose of 0.1–0.2 units/kg/h. By day eight the insulin infusion was discontinued, and she began a subcutaneous insulin regimen with short-acting human insulin and intermediate insulin. Her total daily dose of insulin was 2 units/kg/d. Genetic investigation of the patient was done and we disclosed that the infant was heterozygous for a new missense mutation in the KCNJ11 gene, p.Val252Leu. The patient was one month old at the start of transition from subcutaneous insulin injections to glibenclamide. Treatment was started at a dose of 0.12 mg/kg/d glibenclamide, divided twice daily and her regular insulin was concomitantly tapered off. Her hyperglycemia resolved completely after her glibenclamide dose was further increased to 0.3 mg/kg/d, and she no longer required doses of regular insulin. Two years after starting glibenclamide, the patient was asymptomatic (HbA1c 5.5%), and she was found to be gaining weight (14 kg, +0.9 SDS) and showing normal neurodevelopmental progress at follow-up. The currently glibenclamide dose for this two-year-old girl is 0.4 mg/kg/d (therapeutic range 0.05–1.50 mg/kg/d).
Conclusion: This case illustrates safe and effective initiation of glibenclamide in PNDM due to mutations in K_{ATP} channels.

P-81-047

A novel heterozygous *INS* missense mutation in an infant with permanent neonatal diabetes mellitus presenting with diabetic ketoacidosis

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Objective: Permanent neonatal diabetes mellitus (PNDM) is a very rare condition, affecting around 1 in 260 000 live births in European countries. Recent studies have shown that PNDM, in which diabetes develops in the first few weeks or months of life, is primarily a genetic condition and not a congenital form of type 1 diabetes. Many of these genes are now known and have provided information to improve diagnosis and treatment. An infant with bilateral duplex kidneys and severe scalp alopecia who presented in diabetic ketoacidosis (DKA) was diagnosed with PNDM and was genetically investigated to determine the underlying genetic mutation.
Methods: Sequencing of the *KCNJ11*, *ABCC8* and *INS* genes.
Results: A novel heterozygous missense mutation in the *INS* gene, p.L105P, was identified by molecular genetic testing. The mutation had arisen de novo as both parents were negative on testing.
Conclusion: We describe the first report of a novel p.L105P *INS* mutation in a three month old child with PNDM and a background of bilateral duplex kidneys, non-specific aminoaciduria and profound scalp alopecia. The mutation is in a critical region of the preproinsulin molecule which is predicted to prevent normal folding and progression of proinsulin in the insulin secretory pathway. The child is now thriving with good glycaemic control on a continuous subcutaneous insulin infusion (CSII).

P-95-048

Identification of a novel mutation in an Egyptian infant with Wolcott-Rallison syndrome

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Background: Wolcott-Rallison syndrome (WRS) is a rare autosomal recessive disease caused by mutations in the EIF2AK3 gene. WRS is characterized by neonatal/early-onset non-autoimmune insulin-requiring diabetes which most commonly occurs in populations with high rates of consanguinity.
Case report: We describe a boy, 4th order of birth of consanguineous parents (first degree cousin) who was born at term after an uneventful pregnancy. He was well until the age of 2 months when he was admitted to the intensive care unit with pneumonia. On this occasion, a diagnosis of diabetes mellitus was established by the presence of hyperglycaemia and glycosuria that was treated with ultra short and intermediate acting Insulin. The metabolic control was fair (mean HbA1c was 8.8%). At age of 12 months he started to have progressive abdominal enlargement and sleepiness where on examination the liver was enlarged measuring 6 cm below the right costal margin together with elevated liver function tests (Alt = 305 μ/l, Ast = 315 μ/l), all viral markers were negative. A slight lumbar hyperlordosis, bilateral genu varum was evident and the boy had a broad-based immature toddler's gait. His mental development and motor milestones have remained within normal limits. His sibling (deceased) was also affected with neonatal diabetes at age of 3 months and died shortly by coma but no tests were performed for him. Based on the association between neonatal diabetes, hepatic dysfunction and picture of bone dysplasia WRS was suspected and genetic testing was undertaken. Sequencing analysis identified a novel homozygous missense mutation p.Y213C (c. 638A >G) in exon 4 of the patients EIF2AK3 gene. Both unaffected parents were heterozygous for the mutation.

Conclusion: Genetic counseling for prenatal diagnosis is mandatory in this family as the risk of future pregnancies being affected with WRS is one in four.

P-265-049

Ten cases with diabetes in 1st 6 months of life: clinical, molecular and therapeutic aspects

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Objectives: To study clinical, laboratory, molecular and therapeutic aspects of diabetes presenting in the 1st 6 months of life.

Methods: Ten cases with early diabetes diagnosed and managed at the Diabetes Endocrine and Metabolism Pediatric Unit of Cairo University over a period of one year (Jan–Dec 2011). History and clinical features, laboratory tests on admission and follow up, HLA typing, molecular studies, and mode of therapy are all described. Laboratory: blood glucose, C-peptide, Anti GAD 65, ICA, IAA, HLA DQA1 and DQB1; molecular studies for the common mutations associated with neonatal DM (KCNJ11, INS, ABCC8) and methylation defects. Insulin therapy and efficacy of control (3-monthly HbA1c), frequency of hypoglycemic episodes and growth parameters.

Results: Ten cases with early diabetes (3 in 1st 8 weeks, 7 between 8 and 24 weeks). All presented with ketoacidosis, with disturbed consciousness in 7 with convulsions in 3 cases. All cases had low C-peptide. Only 2 had positive pancreatic antibodies. HLA alleles were protective in 5, predisposing in 3 and combined in 2. Molecular studies revealed methylation defect in 2, KCNJ11 in 3, INS mutations in 2, and no detectable defect in 3. Insulin therapy was instituted in all cases with dose ranging from 0.5–1.5 μ/kg/d. Basal insulin regimen (NPH 2–3 times/day) was more effective in achieving safe control. Insulin was stopped on follow up in 3 cases (Transient Neonatal Diabetes), successfully substituted with sulphonylurea (SU) in 3 cases, and continued in 4 cases (Permanent Neonatal Diabetes, Early T1D).

Conclusion: Infants presenting with diabetes in the 1st 6 months of life are mostly monogenic but T1D is also encountered. Monogenic (neonatal) diabetes can be transient or permanent. Molecular genetic testing is essential in guiding mode of therapy. SU was more effective in achieving diabetes control in cases with KCNJ11 mutation. Basal insulin was more safe in achieving glycemic control in this age group.

P-336-050

Diabetic ketoacidosis at diagnosis: role of family history and class II HLA genotypes

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Objective: To explore the relationship between family history of diabetes and frequency of diabetic ketoacidosis (DKA) at diagnosis and to analyze the possible association between HLA genotypes and DKA.

Methods: 510 children and adolescents aged <17 years with type 1 diabetes (T1D) were recruited. Information on first-degree relative (FDR) history of T1D was collected. DKA and severe DKA were defined as blood pH <7.30 and as pH <7.10 at diabetes onset, respectively. Risk categories for developing T1D were determined according to various HLA DQA1-DQB1 haplotype combinations genotypes. Student's *t* test, Mann-White *U* test and logistic regression analysis were conducted. A *P* value <0.05 was considered statistically significant.

Results: The frequency of DKA and severe DKA at diagnosis was 34.7% and 7.2%, respectively. DKA was more frequent in younger patients (<2 years vs others; 67.6% vs 36.2%, 32.3%, 30.8%; P < 0.001) and occurred less in children with at least one FDR affected by T1D (13.0% vs 37.4%, P < 0.001). The logistic regression showed a significant association between DKA and age at the diagnosis [<2 years; P < 0.01, OR = 1.072 (95% CI 1.024–1.123)] and absence of FDRs with T1D [P = 0.001, OR = 4.287 (95% CI 1.770–10.383)] but not with increased HLA-associated risk genotypes [P = ns, OR = 1.550 (95% CI 0.992–2.423)].

Conclusions: In this study we underline the protective effect of having at least one FDR with T1D in reducing the DKA incidence. Even in children <2 years of age, the presence of a FDR with T1D has a protective effect that results more important even than the HLA-associated high risk genotypes.

P-291-051

Majewski osteodysplastic primordial Dwarfism type II and diabetes type II: case report

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Introduction: Majewski Osteodysplastic Primordial Dwarfism type II (MOPD II) is a rare, autosomal recessive disorder, characterized by severe intrauterine growth retardation, dwarfism, severe microcephaly, skeletal dysplasia. We report a patient with MOPDII combined with type 2 diabetes (DTII).

Case report: The 25 year old patient is from a consanguineous Moroccan family, with a birthweight of 1.5 kg and unknown height. He had microcephaly, extremely short stature (97 cm), skeletal dysplasia, mental retardation, hemiparesia attributed to old strokes. MNR depicted Moyamoya disease with laminar necrosis on the left hemisphere and vessel narrowing in the internal carotid arteries. He had polyuria-polydispia. He had acanthosis nigricans in the neck and in inguinal and periumbilical regions, hypertension, hypercholesterolemia and chronic renal insufficiency with anemia (Hb: 7 g/dl) and proteinuria. Oral glucose tolerance test showed fasting glycemia at 129 mg/dl with a peak at 235 mg/dl (T60) and insulin resistance with a peak at 568 μU/ml). There was no renal artery stenosis. Molecular analysis identified a homozygous mutation in exon 19 in the pericentrin (PCNT) gene. The PCNT gene encodes for a centrosomal protein playing a key role in the mitotic spindles. Mutations in PCNT gene are involved in dwarfism and microcephaly, may have an impact on vascular abnormalities and are associated with severe insulin resistance and diabetes. This extremely short patient depicted the phenotype of this rare disease. Treatment consisted in metformin, atorvastatin, erythropoietin, enalapril.

Conclusion: This 25 year old patient presented a MOPDII disease, with Moyamoya disease, mental retardation, in association with diabetes type II, insulin resistance, hypercholesterolemia, hypertension and chronic renal insufficiency. Prognosis of this pathology is unknown, but the older reported patient is 29 year old.

P-390-052

The genetic factor analysis within the type 1 diabetic children and their families

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Aim: Identification of the HLA alleles in diagnosed type 1 diabetes mellitus (T1DM) children and, also in their non-diabetic family members.
Method: The studied group included 25 T1DM children (lot A) and 28 first degree relatives (parents and / or siblings) of these (lot B). In all patients we determined HLA DQB1 detecting 5 classes of alleles (HLA DQB1*02, DQB1*03, DQB1*04, DQB1*05, DQB1*06). We used for the alleles group between DRB1*01 and DRB1*16, HLA typing INNO-LIPA HLA-B DRB1 tests.
Results: In group A, 24 of 25 T1DM patients were carrying at least one predisposing allele DQB1*02 or DQB1*0302. Depending on the identified allele we found 4 groups: DQB1*02/DQB1*0302 = 10 cases (40%), DQB1*02/DQB1X (X = different from DQB1*0302) = 9 cases (36%); DQB1*0302/DQBY (Y = different from DQB1*02) = 5 cases (20%); DQB1Z/DQB1Z (Z = different from DQB1*02/DQB1*0302) = 1 case (4%). In group B, we considered 4 subgroups: DQB1*02/DQB1*0302 = 2 cases (7,14%); DQB1*02/DQB1X = 11 cases (39,28%); DQB1*0302/DQBY = 3 cases (10,71%); DQB1Z/DQB1Z = 12 cases (42,85%). In lot B we determined also the presence or absence of HLA DR. Considering the HLA DR genotype found we divided the subjects as following: DRX/DRX (DRX = different from DR3 and DR4) = 10 cases (35,71%); DR3/DRY (DRY = different from DR4) = 9 cases (32,14%); DR4/DRZ (DRZ is a allele different from DR3) = 8 cases (28,51%) and DR3/DR4 = 1 case (3,57%). With an 80% and respectively 60%, transmission percent, the HLA allele DQB1*02 and DQB1*0302 are both as diabetogenic as in countries with a higher transmission of the disease, like Sardinia or the Scandinavian countries. Statistically significant differences were noticed in patients who were heterozygous for DQB1*02/DQB1*0302 allele (40% in diabetic probands, and, just 7.14% in their relatives).
Conclusions: In group A 96% were carrying a predisposing allele for T1DM. HLA DQB1*0201 and DQ B1*0302 alleles are almost 4 times more diabetogeneic than HLA DQB1*05.

P-231-053

The role of PTPN22 *C1858T* polymorphism in diabetes mellitus type 1: first evaluation in Greek population

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Objectives: Type 1 diabetes mellitus (T1DM) is an autoimmune multifactorial disease. Protein Tyrosine Phosphatase Non receptor type 22 (PTPN22) gene encodes lymphoid-specific phosphatase Lyp, an inhibitor of T cell activation and emerging anti-autoimmune therapeutic target. PTPN22 *C1858T* polymorphism was associated with T1DM and other autoimmune diseases in populations of Caucasian origin. The aim of this study was the investigation for the first time of association of PTPN22 *C1858T* polymorphism with T1DM in Greek population.
Methods: We studied 100 children and adolescents with T1DM and 105 healthy individuals of Greek origin without family history of T1DM. The polymorphism was genotyped using polymerase chain reaction with restriction fragment length polymorphism. Statistical analysis was performed with IBM SPSS Statistics 19 program.
Results: *C1858*T and T*1858*T genotypes as well as *1858T* allele were found more frequently in patients (9.0% and 5.0%, respectively) than in healthy individuals (5.7% and 3.3%, respectively) but at non statistical significant level. There was not found statistical significant association with gender, age at diagnosis, severity of onset, history of Hashimoto thyroiditis or family history of T1DM.
Conclusions: Increased frequency of *1858T* allele in Greek patients with T1DM than in controls is in accordance with results of similar studies on other populations. The inability to find a statistical significant difference is probably due to the well established low frequency of minor allele in Greek population, indicating the need for larger sample. Therefore, safe conclusions will arise for the expected benefit of future application of Lyp inhibitors on patients with T1D.

P-294-054

Temporary remission of type 1 diabetes in a girl with nephrotic syndrome

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Introduction: Type 1 diabetes (T1D) and nephrotic syndrome (NS) may coexist with a ratio of 1/3 000 000 in children. We reported the case of an 8 year old girl who presented T1D combined to NS.
Case report: At 5 years of age, the patient had a NS treated during 5 month by steroids. Afterwards, remission persisted during 3 years. She presented a relapse and was treated again with steroids. She was referred for hyperglycemia and HbA1c level was 16%. Laboratory results showed: very low c-peptide (0.4 μg/l), severe dyslipidemia, positivity for autoantibodies: IAA 0.6%, ICA 25 JDFU, GADA 24.2%, IA2A 13%. HLA genotype was HLA DQA3-DQB3.2/DQA4-DQB2 (highest relative risk: 31). She was treated with a two daily freemix injection regimen of insulin (0.7 μ/kg/d). Glycemia were stabilised and HbA1c normalised. Two years later, insulin doses were progressively decreased as steroid treatment was weaned. Insulin was stopped after 2 years. HbA1c remained in the normal range. When TID was diagnosed, NS relapsed and steroid treatment was adapted with several relapses when weaning of steroid was attempted. Cyclophosphamide led to complete remission. Even with a low fat diet, dyslipidemia persisted and atorvastatin was started leading to normalisation of the lipid profile. When steroids were stopped, atorvastatin was interrupted with still normal lipid profile.
Discussion: NS is exceptionally combined with TID. This correlation could be due to autoimmunity associated in both diseases. Steroid treatment for NS may have triggered T1D in a genetically predisposed patient. We ignore the duration of the presence of the autoantibodies.
Conclusions: We reported a girl with an auto immune TID, probably triggered by steroid treatment for NS.

P-457-055

Fasting, mild hyperglycemia due to mutation in glucokinase gene in 12 -year-old patient and his family: from laboratory tests to the genetic diagnosis

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Objectives: Glucokinase (GK) acts as a glucose sensor in the pancreatic beta-cell and regulates insulin secretion. Heterozygous mutations in the human GK-encoding GCK gene that reduce the activity index increase the glucose-stimulated insulin secretion threshold and cause familial, mild fasting hyperglycemia, also known as MODY.
Methods: 12-year-old patient without clinical manifestation of diabetes diagnosed due to fasting hyperglycemia. We noticed positive family history of 'type 2 diabetes': father and grandfather of a patient were suffering from diabetes, treated by oral agents and the heart failure (NYHA I/II) and dilated cardiomyopathy in father. The child was born at term, birth weight was 3160 g. The adjustment and infancy period of a child was unbiased and the proper psychomotor development was observed.
Results: The results of OGTT with insulin assessing are as follows: glycemia -0′ 128mg%, 30′ 185mg%; 60′ 177mg%; 90′ 171mg%; 120′ 169mg%, insulin level - 0′ -15.5 MIU/L, 60′- 17.0 MIU/L, 120′- 36.9 MIU/L. HbA1c percentage was 6.2%. Fasting C-peptide was 2.79 ng/ml and C-peptide 120′ after eating was 2.39 ng/ml. ICA, anti-GAD, anti- IA2 autoantibodies were negative. Conducted genetic evaluation confirmed that the patient and his father are heterozygous for the mutation GGC /AGC in the GCK gene. This mutation causes an amino acid residue substitution of G to S at position 44 of the peptide chain glucokinase. The result confirms the diagnosis of MODY diabetes caused by mutations in glucokinase gene GCK-MODY (MODY2).
Conclusions: (i) the presence of mild persistent hyperglycemia in any patient without auto-antibodies should lead to genetic analysis of GCK,
(ii) confirmation of mutation allows the targeting of appropriate treatment (proper diet therapy without pharmacologic agents in such a sort of mutation),
(iii) The OGTT and genetic test for MODY 2 should be considered in descendents when type 2 diabetes and heart disease are recognized in parents.

Poster Tour 1- Diabetes Acute and Chronic Complications

P-33-110

Relation between neurocognitive profile and diffusion tensor imaging in pediatric patients with type 1 diabetes mellitus

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Objective: Abnormalities in white matter may be partly responsible for cognitive dysfunction in Diabetes Mellitus (DM).
Aim: To define the relation between neurocognitive impairment and white matter changes in patients with type 1 DM (T1DM), and its relation with different disease features.
Methods: Twenty children and adolescents with T1DM and 10 healthy age, sex, education, dexterity and total general intelligence matched controls were recruited for neurocognitive assessment and diffusion tensor imaging (DTI).
Results: DTI values were generally lower in patients in most of the studied areas. HbA1c was inversely correlated to Benton visual memory test scores, general intelligence and performance subscales of IQ. Duration of DM was inversely correlated to total intelligence and fractional anisotropy (FA) at optic radiation. Frequency of hypoglycemia was inversely correlated to performance IQ. The frequency of DKA was inversely correlated to Difference correct score of Benton Visual Memory Test. Difference correct score was positively correlated to lower FA at cingulum, corona radiate, optic radiation and splenium. Difference Error score was positively correlated to FA at corona radiate and optic radiation. Wechsler intelligence scale showed no significant difference except for block design and digit span subscales which were worse in patients. This indicates impairment in visual constructive ability and immediate memory. Digit span test was positively correlated to FA at the mid body area. Number of categories completed was positively correlated to FA at the mid brain region. No significant difference in FA of the examined brain tracts in relation to neuropathy.
Conclusion: Neurocognitive decline in patients with T1DM was significantly correlated to changes in microstructure of white matter as evidenced by DTI. These changes are correlated with duration of illness and can be considered a biomarker for central nervous system affection among diabetic patients.

P-341-111

Prevalence of hypoglycemia unawareness in patients with type 1 diabetes

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Objectives: Hypoglycemia unawareness is a serious diagnostic and therapeutic problem. The aim of the study was to determine the prevalence of hypoglycemia unawareness among type 1 diabetic patients.
Methods: The study included 238 patients, with the onset of diabetes before 18 years of age. Mean age of patients was 25.3 ± 5.1 years, age of diagnosis was 10.3 ± 4.7 years, diabetes duration was 15.04 ± 6.6 years. Hypoglycemia unawareness was assessed by questionnaire method using two tests: by Clarke and by Gold. Patients' height, weight, waist circumference and blood pressure were measured. HbA1c, lipid and creatinine levels were examined. Self-control glycemia results were analyzed.
Results: Hypoglycemia unawareness was found in 58 patients (24.4%) using Clarke's test and in 68 patients (28.5%) using Gold's test. For further analysis three groups were distinguished: Group I- patients with hypoglycemia awareness confirmed by both tests (n = 142), Group II- patients with hypoglycemia unawareness confirmed by one test (n = 66) and Group III- patients with hypoglycemia unawareness confirmed by both tests (n = 30). Patients with hypoglycemia unawareness were older (P = 0.040) and had longer diabetes duration (P = 0.014) than patients with hypoglycemia awareness. No statistic difference between the groups in lipid level, waist circumference, creatinine level, BMI, arterial pressure and HbA1c were found. The patients with hypoglycemia unawareness had more glycemia level below 55 mg/dl (P = 0.016). They performed measurements of glycemia more frequently (P = 0.049).
Conclusion: Hypoglycemia unawareness was observed in 40% type 1 diabetic patients. The severity of hypoglycemia unawareness was associated with longer diabetes duration. The patients with hypoglycemia unawareness had more frequent low glycemia level.

P-20-112

Silent diabetic cochleopathy in type 1 diabetes mellitus

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Objective: Our study aimed to detect early asymptomatic hearing affection whether at the level of outer hair cells (OHCs), inner hair cells (IHCs) and or olivo-cochlear bundle and the relationship between these abnormalities and other variables such as diabetes duration, metabolic control, or presence of microvascular complications.
Methods: Seventy five adolescents withT1DM and 33 healthy controls participated in the study. Duration of DM, HbA1c levels, microvascular complications were analyzed. All underwent basic audiological assessment to ensure normal hearing and middle ear function. Other tests comprised: transiently evoked otoacoustic emissions (TEOAEs) testing OHCs, TEOAEs with contralateral suppression (testing the integrity of olivo-cochlear bundle) and threshold equalizing noise (TEN) testing IHCs as evidenced by dead regions within the cochlea.
Results: Early asymptomatic OHCs affection as reflected by partial pass in 33.75% of cases with diminished suppression as compared to 9.1% control group. Eleven patients (7.33%) showed positive TEN Test reflecting resistance of IHCs to hyperglycemic injury. The mean difference in amplitude of TEOAE before and after suppression was higher in diabetics with microvascular complications when compared to diabetic children without complications at all frequencies (P < 0.001 for all). Duration of diabetes and microvascular complications

(nephropathy, peripheral and autonomic neuropathy were not correlated with the lack of suppression except for retinopathy (P = 0.02). In contrast, poor metabolic control was associated with poor suppression (r = -0.44, P = 0.001).
Conclusions: Cochleopathy can be detected in a relatively high proportion of subjects with T1DM in spite of a normal audiometric hearing threshold. It should be considered as early manifestation of diabetic neuropathy which is related to the degree of metabolic control and retinopathy independent of other microvascular complications.

P-185-113

Urinary markers for early detection of microvascular complications in type 1 diabetic children

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Background: N-acetyl-β-d-glucosaminidase (NAG) is a lysosomal enzyme, present in high concentrations in renal proximal tubular cells.
Objectives: The aim of this study is to investigate the urinary outcome of these markers as an early detector of microvascular complications in type 1 diabetic children.
Design and methods: Subjects of this study were divided into two different groups, type 1 diabetic children group which consisted of 67 subjects and control group which consisted of 31. Type 1 diabetic subjects were divided into microalbuminuric and normoalbuminuric. Fasting plasma glucose, total hemoglobin, glycated hemoglobin A_{1C}, blood urea, plasma creatinine, urinary creatinine concentration, urinary levels of micoalbumin, N-acetyl-B-D glucosaminidase (NAG), Gama glutamyl transferase (GGT), Beta-2-microglobulin, Malondialdehyde (MDA) and Reactive carbonyl groups (RCG_S) were measured in type 1 diabetic subjects and control ones.
Results: A significant increase in tubular injury markers of diabetes (GGT, NAG, beta-2-microglobulin) and oxidative stress parameters (MDA, RCG_S) as compared to control subjects was found. Microalbuminuric subjects showed a significant elevatation in the urinary markers including GGT, NAG, beta-2-microglobulin, MDA, RCG_S as compared to normoalbuminuric subjects. The studied urinary tubular enzymes (GGT, NAG), oxidative stress markers (MDA, RCG_S) and β_2 microglobulin showed positive correlations with one another.
Conclusion: The results of this study indroduced the possibility of depending on tubular enzymes (GGT, NAG), oxidative stress markers (MDA, RCG_S) and β_2 microglobulin as an early, reliable, and sensitive predictors for the children diabetic nephropathy. The NAG activity index proved to be the most sensitive parameter, then β_2 microglobulin for early discovering the tubule cells damage.

P-204-114

Comparison of renoprotective effect of different drugs in normotensive microalbuminuric type1 diabetic patients

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Objectives: Early phase of diabetic nephropathy is functionally characterized by an increase in glomerular filtration rate and development of microalbuminuria.
Aim: Aim of this study is to compare in normotensive type 1 diabetic patients with incipient nephropathy the effect on albumin excretion rate of an ACE inhibitor and two different angiotenzin receptor blockers.
Materials and methods: Forty-two normotensive type 1 diabetic patients (age 24.6 ± 8.3years, 23 female, duration of diabetes 9.8 ± 4.6 years) were included into prospectively randomized clinical trial of 12 months. Patients were grouped randomly into one of the regime of treatment with enalapril 5 mg daily, or losartan 50 mg daily, or valsartan 80 mg as group 1, 2 and 3 respectively. After grouping the patients with microalbuminuria, they were reevaluated with regard HbA1c levels and urinary albumin excretion rates at 4 month intervals for 12 months.
Results: Fifteen normotensive type 1 diabetic patients were treated with enalapril, 14 with losartan and 13 with valsartan. In the enalapril group, all of the patients decreased their albumin excretion to normal levels while 13/14 patients in the losartan group and 12/13 patients in the valsartan group could normalize their albumin excretion. These changes in the albumin excretion rates among three groups did not reach statistical significance during the 12-months of follow up period. There was no significant effect on ambulatory blood pressure.
Conclusions: The data document that ACE inhibitors and two different angiotensin II receptor blockers have similar efficacy in treating diabetic incipient nephropathy.

P-214-115

Juvenile fibromyalgia among children with type1 diabetes mellitus in Ismailia City, Egypt

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Background: Juvenile Fibromyalgia (JFM) is an idiopathic chronic pain syndrome. The current concept views FM as the result of central nervous system malfunction, resulting in amplification of pain transmission and interpretation. Many musculoskeletal abnormalities have been reported in DM.
Objective: To evaluate the frequency of JFM in pediatrics with DM.
Subjects and methods: It is a case-control study. Sixty two children with type I and 62 healthy children age and sex matched were included in the study. The study was conducted at Suez Canal University Hospital, Ismailia. The diagnosis of JFM was based upon criteria developed by Yunus and Masi. Children who suffered from numbness, motor (MCV) and sensory (SCV) nerve conduction velocity studies were performed. Motor nerve conduction of the median, ulnar, peroneal and posterior tibial nerves was performed. The SCV of the median and ulnar nerve was done.
Results: Fibromyalgia was diagnosed in 8 DM patients (13%) and in only one (2%) healthy control (P = 0.008*). DM patients with JFM had significantly higher mean of number of tender point than those without FM (7 ± 2 vs 3 ± 1, respectively) (P < 0.05) Results of electrophysiological studies revealed a significant difference in common peroneal and posterior tibial between diabetic without fibromyalgia and those with fibromyalgia.
Conclusion: In conclusion, we have found an increased prevalence of JFM among chldren with T1DM; therefore JFM can be added to the list of complications associated with T1DM.

P-478-116

Assessment of urinary monocyte chemoattractant protein-1 in children and adolescents with type 1 diabetes mellitus

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Objectives: Diabetic nephropathy is the leading cause of end stage renal disease worldwide. In the presence of high concentrations of glucose and advanced glycation end-products, renal tubular epithelial cells have been shown to produce monocyte chemoattractant protein-1(MCP-1). This study aimed to examine the level of urinary MCP-1 as marker for development of diabetic nephropathy in children and adolescents with type-1 diabetes mellitus (T1DM) in addition to assessing its relation with glycemic control, duration of disease and microalbuminuria.
Methods: After informed consent, 52 patients with T1DM (mean age 13.92 ± 3.17 years) were recruited from Diabetes Clinic. Fifty healthy children and adolescents matched in age (mean age 12.8 ± 3.12 years), gender, BMI and pubertal stage served as control group. The participants were subjected to clinical evaluation and measurement of mean HbA1c, urinary microalbumin, urinary creatinine and urinary MCP-1 by ELISA technique.
Results: There was significant increase in urinary microalbumin (38.81 ± 34.290 vs 5.54 ± 3.34 mg/dl) and urinary MCP-1 (283.96 ± 130.470 vs 36.84 ± 20.81 pg/dl) and significant decrease in urinary creatinine (83.06 ± 13.763 vs 130.36 ± 28.88 mg/dl) in patients with T1DM compared to controls($P < 0.001$). Urinary MCP-1 level showed a highly significant positive correlation with HbA1c% ($r = 0.611$, $P < 0.001$)and urinary microalbumin ($r = 0.459$, $P < 0.001$) and a significant negative correlation with urinary creatinine ($r = -0.600$, $P < 0.001$). Urinary MCP-1 had no correlation with age, age at onset or duration of diabetes. Thirty four studied diabetic patients with urinary MCP-1 level above110pg/dl had normoalbuminuria.
Conclusions: Urinary MCP-1 may have a predictive value as a non invasive marker of diabetic nephropathy. It may appear in urine before microalbumin and its rise may be related to poor glycemic control.

P-100-117

Can optical coherence tomography (OCT) predict early retinal microvascular pathology in type 1 diabetic adolescents but no diabetic retinopathy? A single centre study

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Background: Optical coherence tomography (OCT) has been proven useful in measuring retinal thickness and volumes in patients with diabetes.
Objective: To test whether OCT is able to identify early retinal changes and potential correlations with metabolic parameters and other microvascular complications.
Patients and methods: Thirty patients with T1DM without minimal diabetic retinopathy (MDR) (17 males, 13 females, aged 14.3 ± 2.4 years) compared with age-matched healthy volunteers were examined with OCT. Diabetes duration, anthropometric measurements, HbA1c, other microvascular complications (nephropathy autonomic and peripheral neuropathy) and total cholesterol were determined.
Results: No statistical significant differences was found between patients with ($n = 15$) and without microvascular complications ($n = 15$) compared to controls regarding retinal volume, nerve fibre layer volume (temporal and nasal quadrants) and ganglion cell volume in both eyes ($P > 0.05$ for all). No correlation was found between ganglion cell layer volumes and clinical and laboratory characteristics of the patients except negative correlation with total serum cholesterol($r = -0.369$, $P = 0.049$). Best cut off value of ganglion cell layer volume to detect the level at which thinning of this layer occurs was >1900 microm.
Conclusion: Our study suggests that no advantage in performing OCT routinely in patients with T1DM without MDR. OCT seemed not to be useful for the detection of early MDR in patients with no clinical evidence of macular edema. Therefore, the conventional diagnostic methods are mandatory to detect early diabetic retinopathy.

P-160-118

System dysfunction blue-sensitive cones (S-cone) in children and adolescents with type 1 diabetes without clinical features of diabetic retinopathy

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Objectives: In the literature there are reports of impaired function of shortwave cones in response to retinal hypoxia. Aim of the study was to determine whether the short wavelength sensitive (S) cone electroretinogram. (ERG) is selectively altered in young patients with and without long-lasting diabetes.
Methods: Study group consisted of 31 patients with type 1 diabetes It was divided into a group of diabetes t. 1 lasted >10 years ($n = 13$, 26 eyes) and the group with diabetes t.1 within 5–10 years of disease ($n = 18$, 36 eyes). The control group consisted of 16 eyes ($n = 8$). Based on ophthalmoscopy and fluorescein angiography we excluded the presence of changes in the eye and made the S-cone ERG. Stimulated retinal response to stimuli in both eyes 0.1, 0.2, 0.5 cd x s/m^2.
Results: In our study we observed a reduction in an average electroretinogram b wave amplitude in response to a stimulus 0.2 cd xs/m^2 in the group with diabetes t. 1 compared with the control group (38.91 ± 11.16 vs 45.10 ± 10.2) ($P < 0.05$). It obtained a reduction of the average amplitude of the wave b in response to a stimulus 0.5 cd xs/m^2 in the group with diabetes t. 1 compared with the control group (69.53 ± 19.09 vs 83.0 ± 18.3) ($P < 0.02$). Comparing the different groups of patients with diabetes t.1 and a control group found that the average amplitude of the a wave and 0.5 cd xs/m^2 response was significantly reduced in the group with diabetes >10 years relative to the control group (-17, 16 ± 12.8 vs -26.23 ± 8.92) ($P < 0.02$).
Conclusion: In summary, the finding is that the S-cone ERG could be a helpful test assessing early retinal dysfunction in young patients with long lasting diabetes.

P-463-119

Assessment of endothelial dysfunction in children and adolescents with type 1 diabetes

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Background and aims: Being the earliest step on the way to atherosclerosis' development, endothelial dysfunction is particularly escalated in diabetes. This study aimed at assessing endothelial dysfunction in young patients with T1DM and defining clinical factors that influence it.
Material and methods: The study group comprised 52 children and adolescents aged 14.07 ± 3.03 years, with T1DM duration 5.13 ± 2.18 years. Controls were 20 healthy age- and sex-matched peers. A medical history obtaining: physical examination and laboratory test i.e. blood lipids (total cholesterol, LDL, HDL, TG), chosen markers of endothelial damage (sICAM, sVCAM, sE-selectin, TNF-α, IL-6) as well as ambulatory blood pressure monitoring (ABPM) were performed in all subjects.
Results: Patients with T1DM displayed significantly higher concentrations of chosen markers of endothelial dysfunction compared to controls (sVCAM (ng/ml): 951.56 [856.58 ÷ 1046.55] vs 710.35 [627.00 ÷ 793.71], TNF-α (pg/ml): 16.63 [14.24 ÷ 19.02] vs 9.41 [7.42 ÷ 11.39], IL-6 (pg/ml): 3.38 [2.99 ÷ 3.78] vs 2.45 [2.05 ÷ 2.85]; $P < 0.05$). Diabetic subjects with an abnormal ABPM reading had significantly higher concentrations of sE-selectin. The study revealed a significant positive correlation between sE-selectin and systolic as well as diastolic pressure load during the day period.
Conclusions: The status of endothelium in children and adolescents with T1DM assessed by means of chosen biochemical markers differs significantly with that in their healthy peers which points at endothelial dysfunction. It seems to be in relation with disturbances of blood pressure.
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P-363-120

Affecting factors on ratio of glycated albumin to hemoglobin A1c in Japanese children and adolescents with type 1 diabetes

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Objective: In children and adolescents with type 1 diabetes mellitus (T1DM), we simultaneously measured glycated albumin (GA) and A1C to elucidate factors that affect the GA/A1C ratio.
Methods: In 752 T1DM patients for ≥6 months duration of the 3rd cohort of the Japanese Study Group of Insulin Therapy and 62 non-diabetic siblings, GA and A1C were measured. Body mass index SDS (BMI-SDS), basal-bolus (MDI) therapy or not, insulin dose per body weight (I/kg) and bolus insulin dose (bolus %) were selected as explanatory factors. A1C was expressed by NGSP number. Otherwise A1C (SI) was specified, when IFCC number was applied for HbA1c value.
Results: The patients' age was 12.1 ± 3.8 years, and disease duration was 7.0 ± 3.8 years. A1C was 7.9 ± 1.2%, GA was 23.9 ± 5.2%, and the GA/A1C ratio was 3.03 ± 0.31. GA/A1C ratio has positive association with age ($P < 0.0001$) and negative association with BMI-SDS ($P < 0.005$). Between the non-MDI group (108 patients) and MDI group (644 patients), GA and BMI-SDS were not different; but in the MDI group, A1C was significantly lower ($P < 0.005$), age was older ($P < 0.0001$), disease duration was longer ($P < 0.01$), and I/kg was higher ($P < 0.005$). GA/A1C ratio has positive correlation with A1C (GA/A1C = 2.430 + 0.076*A1C, $P < 0.0001$) but negative correlation with A1C using IFCC values (GA/A1C (SI) = 0.425–0.001*A1C (SI), $P < 0.0001$). GA/A1C in T1DM was significantly higher using NGSP values (3.03 ± 0.31 vs 2.6 ± 0.21, $P < 0.0001$), but lower using IFCC values than siblings (6.95 ± 0.71 vs 7.13 ± 0.72, ns). In multiple regression analysis, the GA/A1C ratio was positively correlated with age and A1C, and negatively correlated with disease duration, BMI-SDS, and I/kg, while the GA/A1C (SI) ratio was negatively correlated with A1C(SI).
Conclusion: In children and adolescents with T1DM, the GA/A1C ratio decreases with increasing obesity and higher insulin doses. In addition, the GA/A1C ratio becomes relatively higher at higher A1C ranges using NGSP value, which should be kept in mind.

Poster Tour 2 - Diabetes Acute and Chronic Complications

P-236-077

Thyroid pattern at type 1 diabetes mellitus (T1DM) onset: prevalence and follow up in a pediatric population

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Background: The nonthyroidal illness syndrome (NTIS) is a condition characterized by abnormal TSH and thyroid homone levels and it is frequently reported during severe illness, as at T1DM onset.
Objective: To study thyroid function at T1DM onset and after 2 years.
Methods: We examined 149 pts (72 M and 77 F, mean age 7.7 ± 4.1 years) diagnosed for T1DM from 2000 to 2011. Besides standard DKA assessment, we evaluated hypothalmus-pituitary-thyroid and adrenal axis and antiTG/TPO Ab.
Results: Twenty patients were positive for at least one anti-thyroid Ab (group A), the remaining patients were negative for both (group B). We subdivided the 2 groups in 4 subgroups according to thyroid pattern: Group A: 10% had hypertireotropinemia, 26% had low fT3 levels, 5% had low fT3 and fT4 and 53% were normal Group B: 6% had hypertireotropinemia, 24% had low fT3 levels, 19% had both low fT3 and fT4 and 51% were normal. No significant differences in thyroid pattern at T1DM onset according to antithyroid Ab were found. Multiple regression analysis identified BE (R^2 = 0.38; P < 0.0001) and fructosamine (R^2 change=0.12; P < 0.0001) as major influencing variables on fT3 levels.
After 2 years thyroid levels remained pathological in 33% of group A and in 2% of group B (P = 0.006).
Conclusion: Abnormalities in thyroid pattern are frequent at T1DM diagnosis regardless of auto-Ab positivity. Thyroid function is strictly related to severity of metabolic pattern. Impaired thyroid levels showed longer duration in pts with antithyroid-Ab suggesting organic dysfunction.
Table: Data at onset (whole gruop).

	Normal thyroid function (77 pts)	Pathological thyroid function (72 pts)	P
BMI SDS	-0.28 ± 1	-1.02 ± 1.1	<0.0001
HbA1c (%)	11.14 ± 2.3	12.5 ± 2.1	<0.0001
Fructosamine (μmol/l)	559.27 ± 135.2	680.73 ± 146.8	<0.0001
pH	7.32 ± 0.1	7.22 ± 1.3	<0.0001
BE	-3.95 ± 8.4	-12 ± 10	<0.0001
Aldosterone (ng/dl)	271.55 ± 238	760.3 ± 751.4	<0.0001
Cortisol (μg/dl)	155.76 ± 84.6	240.3 ± 133.6	<0.0001
C-peptide (ng/ml)	0.73 ± 0.5	0.46 ± 0.3	<0.0001

P-58-078

Demographic characteristics and autoimmunity in familial type 1 diabetes

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Background: Familial type 1 DM is associated with other autoimmune endocrine disorders.
Objectives: To study clinical and demographic characteristics of familial type 1 DM aiming to evaluate difference between index and second affected cases and compare between familial and sporadic type 1 DM cases.
Methods: Demographic and clinical data were collected from 25 families with more than one affected member of type 1 DM (19 sib-pairs and 6 parent-offspring families) comprising 50 type 1 diabetic patients and were compared to 40 sporadic type 1 diabetic cases matched by age, gender, and year of diagnosis. Laboratory investigations included: HbA1c, fasting C-peptide, thyroid autoantibodies (antimicrosomal and antithyroglobulin Abs).
Results: There was higher prevalence of Sibling families than parent offspring families (76% vs 24%). Demographic and clinical data were similar between familial and sporadic cases but C-peptide was significantly higher among familial cases (P = 0.001). Anti thyroid antibodies were significantly higher in familial cases compared to sporadic cases (P = 0.04) and more in siblings than parent-offspring. Dose of insulin was significantly higher among thyroid autoantibody positive familial cases compared to negative ones (P = 0.002). Second affected cases appeared to be younger in age, with higher initial C-peptide, better glycemic control, less incidence of DKA and less insulin dose, however not to a statistical difference.
Conclusion: Autoimmune thyroid (AIT) disease is more common among familial type 1 diabetes cases than sporadic cases, especially among sibling families and particularly affecting females. Insulin requirements are usually increased when diabetes is associated with AITdiseas. Second affected cases appear to have better glycemic control than index cases due to earlier recognition of the disease by experienced parents or relatives and raised awareness which is critical in earlier diagnosis and preventing metabolic derangements.

P-36-079

Assessment of serum protease inhibitors: alpha 1 antitrypsin and antithrombin III in Egyptian adolescents with type 1 diabetes

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Background: Alpha 1 antitrypsin(AAT) and antithrombin III(AT)are serine protease inhibitors which control activities of proteolytic enzymes. These enzymes play a key role in coagulation, fibrinolysis, kinin and complement activation.
Objectives: To assess levels of two serum protease inhibitors: AAT and AT in adolescents with type 1 diabetes as predictors for the development of diabetic microangiopathy and possible correlation with diabetes duration and glycemic control.

Methods: The study included 64 adolescents with type 1 diabetes (mean age 14.53 ± 2.2 years, 42 males and 22 females) and 40 healthy adolescents,age and sex matched as controls. Patients were subdivided into 40 with diabetic microvascular complications (MVC) and 24 without MVC. All participants were subjected to history taking and clinical examination. Laboratory investigations included glycated hemoglobin (HbA1c), urinary albumin excretion (UAE), serum alpha 1 antitrypsin and antithrombin III enzyme assay.
Results: Mean AAT was significantly lower in patients compared to controls (125.97 ± 35.21 mg/ml & 175.3 ± 34.23 respectively, P = 0.0006) and in patients with MVC (94.92 ± 13.44) in comparison to those without MVC (144.6 ± 20.71) (P = 0.0001). Diabetic patients showed significantly higher mean AT (27.45 ± 5.13 mg/ml) compared to the control group (22.56 ± 3.3 mg/ml, P = 0.0008). Patients with MVC had significantly higher level of AT as compared to those without MVC (31.8 ± 4.94 mg/ml & 24.84 ± 3.11, P = 0.002). A significant positive correlation was found between AT and diabetes duration, HbA1c and UAE(r = 0.38, 0.36, and 0.40 respectively).
Conclusion: Serum trypsin inhibitor changes and protease-antiprotease imbalance occur in adolescents with type 1 diabetes and may have a role in development of diabetic MVC.

P-15-080

Diabetic ketoacidosis, determinants and mortality rate in Sudanese children with type 1 diabetes mellitus

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Background: DKA is common at diagnosis in children with T1DM, and has significant morbidity and mortality. Many risk factors were implicated in its development and degree of severity.
Objectives: To describe the frequency of DKA at the onset of T1DM, identify the determinants of DKA, assess its severity, and determine its mortality rate in children in Sudan.
Methods: Hospital records of 466 diabetic children up to 18 years of age, diagnosed during the period 2006–2010 were reviewed (Gaafar Ibn Auf Children's Hospital, Khartoum). DKA was assessed mainly clinically using the severity criteria of Endocrine Clinics of North America 2000. Data were analyzed using the SPSS version 18. The differences in the mean values were calculated using the ANOVA test. Pearson's correlation coefficient was used to evaluate the relationship between variables. For all tests, P < 0.05 was accepted as significant.
Results: Of all patients diagnosed with T1DM, 173 (37.1%) presented with DKA in the latest admission. The frequency of DKA in newly diagnosed children was 35.2%. The majority had either mild (50%) or moderate DKA (37.2%). The frequency of DKA was higher in older children (P < 0.05). The major precipitating factors were infection (56.0%), omission of insulin dose (25.6%) and low socioeconomic status (21.8%). There was a significant positive relationship between age groups and HbA1c levels (P < 0.0001). Moreover, girls had significantly higher latest HbA1c levels (P < 0.003). Two children died (0.4%).
Conclusion: Our study provides recent data in East African population, for whom data are sparse. The incidence of DKA at initial presentation of T1DM among children in Sudan is high due unawareness of the population. Older children with T1DM face an increased risk for developing DKA, due to frequent omission of insulin doses and problems of non-compliance. Intensive educational programs about the early symptoms of diabetes will reduce the frequency of DKA in new patients.

P-26-081

Pulse pressure in children and adolescents with type 1 diabetes mellitus in Germany and Austria

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Background: Impaired blood pressure regulation contributes to the development of diabetic complications. The influence of systolic (SBP) and diastolic blood pressure (DBP) is still controversial. Peripheral pulse pressure (PP), the difference between SBP and DBP, is an indicator for arterial stiffness. T1DM causes increased arterial stiffening and advanced vascular aging in adult patients. However, little data are available for PP in children. Therefore, we studied PP regulation in type 1 diabetic children.
Methods: Blood pressure values of 47153 patients with T1DM <20 years are documented in the DPV database. The average blood pressure of the most recent year was calculated and patients with antihypertensive medication were excluded. Blood pressure values of the diabetic patients were compared with the control populations of the ''4th report on high blood pressure in children (4th report)'' and the German KIGGStudy.
Results: Pulse pressure levels are significantly elevated in diabetic children (PP T1DM 49.13 ± 11.1 vs 4th report 45.38 ± 3 and KIGGS 44.58 ± 4.6 mmHg (all P < 0.0001, Wilcoxon test). PP is increased in 63% (4th Report) or 67% (KIGGS) of the patients, respectively. Absolute PP is elevated independently of the control population and increases with age in both sexes. The rate of increased PP remains stabile between 59 and 68%, irrespective of sex, age and the control population. Age, male sex, diabetes duration, insulin dose, BMI, and height are independent factors contributing to elevated PP levels and to a higher rate of increased PP. HbA1c is only related to increased PP levels (multiple linear regression).
Conclusions: Increased PP in type 1 diabetes is a marker for accelerated arterial stiffness and aging and should be considered as an additional risk factor in the treatment of diabetic children. The elevated PP values in children and adolescents with type 1 diabetes may contribute to their markedly high risk for early development of atherosclerosis.

P-432-082

Leptin level and chronic complications in children with type 1 diabetes mellitus

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Introduction: Type 1 diabetes mellitus is one of the most common chronic diseases in children. Precise knowledge of the pathogenesis of diabetes mellitus type 1 and its chronic complications is the enormous challenge in modern diabetology. In recent years, the role of leptin in the pathogenesis of

microvascular diabetic complications has been highlighted. The aim of the study was to investigate serum leptin level and correlations between leptin levels and clinical and biochemical parameters in patients with diabetes mellitus.
Materials and methods: The study included 130 patients with DM1, lasting 6.05 ± 3.25 years, aged 14.37 ± 3.13 years from Clinic of Pediatrics, Hematology, Oncology and Endocrinology, Medical University of Gdansk and 50 controls. Patients with type 1 diabetes mellitus were divided in two subgroups with and without late diabetic complications. In all children HbA1c, C-reactive protein, lipid profile, albuminuria and serum leptin level with enzyme immunoassay were performed.
Results: Statistically significant differences in leptin level, among patients with long-term type 1 diabetes (7.63 ± 8.41 ng/ml) and group of healthy children (9.58 ± 6.61 ng/ml) were shown with the highest level in control group (P = 0.04). In patients with symptoms of late diabetic complications were significantly higher levels of leptin (9.88 ± 8.74ng/ml) compared with patients with DM1 who have no signs of diabetic nephropathy or retinopathy (7.15 ± 7.91 ng/ml) (P = 0.03). In addition, patients with long-term type 1 diabetes showed significant positive correlations between leptin level and C-reactive protein level (r = 0.21; P = 0.02).
Conclusion: Increasing serum leptin level in children with long-standing DM1 and its positive correlation with C-reactive protein suggests a growing body inflammatory reaction in these patients and may predispose them to the development of diabetic microangiopathy.

P-417-083

The analysis of indicators endotehelin 1-21 in whey of blood and indicators of daily monitoring of arterial pressure with a diabetic nephropathy at children and the teenagers sick of a diabetes of 1 type

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Objectives: To identify markers of vascular damage and to assess blood pressure at different stages of diabetic nephropathy in children and adolescents with diabetes of the 1st type.
Methods: The basic group amounted to 79 patients aged 10–18 years (15.9 ± 2.17). They were divided into 3 groups: the 1st-with normalalbuminuria (n = 31), 2-with microalbuminuria (n = 32), 3-with proteinuria (n = 16). The control group consisted of 16 healthy children and teenagers of the same sex and age. Complex clinical-laboratory study of patients used standard methods of research. BP monitoring was performed by «Shiller BR-102 plus». The level of endothelin1-21-by ''ELISA'', «BIOMEDICA (0.26 fmol/ml). The results are processed in the program Microsoft Excel (2007), STATISTICA 6.0 (StatSoft).
Results: Percentage of children with stable hypertension increased with the progression of DN. Patients with microalbuminuria and proteiuria have higher average daily, daytime and nighttime SBP and DBP. The increased variability of individual values of SBP were recorded in 17.6% in the group with normalalbuminuria, the 39.1% -with microalbuminuria, and 42.9% -with proteiuria, diastolic blood pressure- at 11.8%, 34.8%, and 42.9%, respectively. 47.1% of children and adolescents 1st group, 72.7% - the 2nd group and 75% - the 3rd group didn't have an adequate BP at night. Higher levels of ET1-21 shows the progression of endothelial dysfunction in patients with type 1 diabetes as the formation of of diabetic nephropathy.
Conclusions: In children and adolescents with type 1 diabetes labile hypertension was in 34.1%, stable - at 25.5%. We found a connection between the progression of diabetic nephropathy and elevated levels of endothelin-21 at the stages of microalbuminuria and proteiuria. The interrelation between the level of endothelin1-21 and diastolic blood presure, indicating the role of endothelial dysfunction in the development of DN, the initial changes in the profile of blood pressure.

P-319-084

Cardiac autonomic neuropathy in children with diabetes mellitus

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Objective: Autonomic neuropathy is a severe chronic complication of diabetes mellitus, which worsens life expectancy. Its subclinical state could be established earlier in the course of the disease.
Methods: We investigated 214 children and adolescents aged 7–20 years with history of Insulin dependent diabetes 3–16 years and 346 controls. Heart rate variability (HRV) was measured by Time-domain and Frequency-domain analysis of R-R intervals of ECG in steady-state conditions and during sympathetic and vagal stimuli. Deviations of results out of referent intervals (25–75 percentile) and standard deviation scores (SDSs) were assessed for heart rate (HR), Coefficient of variation (CV) at rest, HRV during deep breathing and expiratory maneuver of Valsalva, total power (TP), LF/HF at rest and TP during orthostatic load. Diabetic children were divided then in to 7 clinical groups: 1 to 5 according personal mean HbA1c from 6% to ≥10%; 6th group: mean HbA1c ≥10% and diabetic late complications; 7th group: HbA1c ≥10%, late complications and growth retardation.
Results: Group 7 had the longest history of diabetes (12.5 ± 3.05 years vs 3.81 ± 1.64 years for group 1, P < 0.05). The values below 25 percentile for TP and CV at rest, DB, Valsalva and TP during orthostasis and values higher than 75 percentile for HR and LF/HF at rest existed in all groups, but their number increased gradually up to 100% in the 7th group. Within the groups 1 to 5 the differences of mean SDSs were non significant irrespective of their mean HbA1c (P > 0.05). Mean SDSs of TP at rest and Valsalva in groups 6 and 7 were statistically different from groups 1 to 5 for (P < 0.05). HR, LF/HF and CV at rest, DP and TP during orthostasis outlined significantly only the 7th group against the others (P < 0.05).
Conclusion: Subclinical cardiac autonomic neuropathy coexisted together with late diabetes complications and growth retardation in children due to longer than 10 years exposition of poor glycaemic control.

P-107-085

Carotid artery intima-media thickness in pediatric type 1 diabetic patients

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Objectives: To compare the carotid artery intima-media thickness pediatric type 1 diabetic patients against that in healthy control subjects matched for age, sex, height, weight, body mass index(BMI) and waist circumference.

Methods: The evaluation consisted of anthropometric measurements, biochemical parameters, and a carotid Doppler and real-time ultrasound, in which carotid artery intima-media thickness (cIMT), flow-mediated dilation (FMD) and carotid stiffness index were measured using standardized procedures.
Results: A total of 50 diabetic patients and 45 control subjects were included. There were no significant differences in the groups for age, sex, height, weight, BMI and waist circumference. (mean age 12.10 ± 2.02 vs 11.49 ± 1.90 years, weight 41.14 ± 11.28 vs 40.88 ± 11.68 kg, height 149.78 ± 20.3 vs 145.62 ± 20.14 cm, BMI 18.49 ± 2.64 vs 18.26 ± 2.59 kg/m^2, waist circumference 69.72 ± 8.6 vs 66.05 ± 7.47 cm, respectively). The diabetic group had higher serum total cholesterol and VLDL cholesterol concentration compared with control subjects (165.9 ± 38.8 vs 130.4 ± 25 mg/dl total cholesterol; $P < 0.001$ and 13.32 ± 8.48 vs 10.22 ± 2.76 mg/dl VLDL cholesterol; $P = 0.018$). A significantly higher cIMT was found in the patients with type 1 diabetes (0.49 ± 0.05 vs 0.44 ± 0.03 mm; $P < 0.001$). A higher carotid stiffness index was found in the diabetic group when compared with control group (3.11 ± 0.46 vs 2.6 ± 0.29 mm; $P < 0.001$).
Conclusions: Type 1 diabetes is associated with higher cIMT and carotid stiffness index in a pediatric population.

P-23-086
Relationship between glucose excursion and activation of oxidative stress in children with type1 diabetes mellitus

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Objective: To explore the correlation between glucose excursions and oxidative stress in children with type 1 diabetes mellitus.
Methods: Using a prospective design, 25 newly diagnosed T1DM inpatients identified from May 2010 to January 2011 and 25 healthy controls matched for age and sex were treated with CSII and monitored by CGMS. 24h urine samples were collected for concentration of 8-iso prostaglandin F2α(8-isoPGF2α) to evaluate the level of oxidative stress using ELISA method. Patients collected 7th day to 9th day 24h urine since admitted, while 25 healthy controls collected one 24h urine. Intraday glycemic excursion was assessed by MAGE, LAGE, SDBG and number of glycemic excursions (NGE). The correlation between glucose parameters (MBG, MAGE, SDBG, LAGE, NGE) and index of oxidative stress were calculated.
Results: 24h urine 8-isoPGF2α in T1DM group (882.20 ± 439.86 ng) was increased as compared with control group (639.41 ± 361.47 ng) ($P < 0.05$). Univariate regression did not reveal an association for MAGE, LAGE, SDBG or NGE with 24h urine 8-isoPGF2α, nor was an association revealed when corrected for HbA1c, age, sex. Spearman correlation between 24h urine 8-isoPGF2α and MAGE, LAGE, SDBG and NGE were non-significant.
Conclusions: We report that there is no relationship between glucose variability and 24h urine 8-isoPGF2α. We also confirm that children with type 1 diabetes have higher levels of 24h urine 8-isoPGF2α than healthy controls.

P-304-087
Clinical detection of peripheral and autonomic neuropathy in type 1 diabetes: are bedside tests reliable?

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Objectives: To assess the reliability of simple bedside tests in detection of peripheral and autonomic neuropathy in type 1 diabetes.
Methods: Sixty children and adolescents wit type 1 diabetes (duration 1.1–23.9 years) were included. After careful inquiry of symptoms suggestive of peripheral and autonomic neuropathy, each patient was tested by a single observer for peripheral neuropathy (PN) using four bedside screening tests (pin prick, light touch, vibration and pressure tests), and for autonomic neuropathy (AN) by evaluating resting pulse for tachycardia, and supine followed by standing blood pressure for postural hypotension. Nerve conduction studies were done after explanation and patient's consent: motor nerve conduction for the left common peroneal nerve, right posterior tibial nerve and the right ulnar nerve; and sensory nerve conduction for the left sural nerve and the left ulnar nerve in addition to upper limb sympathetic skin response.
Results: Neuropathy was detected clinically in 22 patients, PN in 6, AN in 8, and combined PN and AN in another 8. Fifty patients agreed to do nerve conduction studies, 5 with PN, 6 with AN, 8 with combined PN and AN, and 31 with no clinically detectable neuropathy. Abnormal nerve conduction velocities were found in 15 out of the 19 cases with clinically detectable PN and/or AN, and in 3 out of the 31 clinically free cases. Sensitivity and specificity of the individual bedside tests ranged from 40 to 73.33% and from 91.43 to 97.14% respectively. Combining the 4 tests for PN had a sensitivity of 73.33%. Resting tachycardia and postural hypotension had a sensitivity of 72.73 and 27.27%, and specificity of 84.62 and 100%, respectively.
Conclusion: Combined 4 bedside tests, resting tachycardia and postural hypotension showed low sensitivity in detecting peripheral and autonomic neuropathy when compared with standardized electrophysiological tests.

Poster Tour 3 - Diabetes Acute and Chronic Complications

P-345-099

Relationship between oxidative stress markers and carotid intima media thickness in type 1 diabetic children and adolescents

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Objectives: Carotid intima media thickness (CIMT) is a non invasive marker of subclinical atherosclerosis. Hyperglycemia, oxidatively modified atherogenic lipoproteins and advanced glycation end products are linked to increased oxidative stress in diabetes. We aimed to find out the relation between carotid intima media thickness in type 1 diabetic children and adolescents and plasma nitric oxide and total antioxidant capacity levels as markers of oxidative stress.

Methods: This study included 50 children and adolescents with type 1 diabetes mellitus with mean age 9.7 ± 3.4 years and 50 healthy age and sex matched controls. Their duration of illness ranged from 1–13 years. They were subjected to assessment of hemoglobin A1c, total cholesterol and triglycerides, plasma total antioxidant capacity, serum nitric oxide by colorimetric method and carotid intima media thickness by high-resolution B-mode ultrasound.

Results: There was significant elevation in nitric oxide (17.07 ± 6.4 vs 12.6 ± 4.7 μmol/l; $P < 0.001$) and CIMT (0.47 ± 0.04 vs 0.39 ± 0.02 mm; $P < 0.001$) and significant reduction in total antioxidant capacity (0.41 ± 0.29 vs 0.87 ± 0.23 mmol/l; $P < 0.001$) in diabetic patients compared to controls. Carotid intima media thickness was correlated positively with nitric oxide ($r = 0.402$, $P = 0.01$) and negatively with total antioxidant capacity ($r = -0.341$, $P = 0.02$). Carotid intima media thickness was also correlated positively with age, duration of diabetes but not correlated with glycemic control or lipid profile.

Conclusions: The significant elevation in nitric oxide and reduction in total antioxidant capacity in children and adolescents with type 1 diabetes mellitus together with their correlation with carotid intima media thickness may reflect the role of oxidative stress in the development of atherosclerosis in young type 1 diabetic subjects.

P-494-100

ADAMTS-13 a noval marker linking between micro and macro-vascular complications in young type-1 diabetics

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Objectives: To determine whether a correlation existed between the thrombotic tendency, as measured by ADAMTS-13 levels and diabetic microvascular as well as macrovascular complications measured as dyslipdemia and carotid intima media thickness(CIMT).

Methods: Seventy type 1 diabetics were compared with 40 healthy controls. The mean age of patients was 12.6 ± 4.9 years.Medical history with special emphasis on disease duration and insulin therapy, clinical examination, blood pressure measurement, as well as screening for diabetic complications, was performed. Laboratory assessment of high-sensitivity CRP, Lipid profile, albumin/creatinine ratio, renal functions and HbA_1c were assayed. Carotid intima-media thickness (cIMT) as well as ADAMTS-13 level using ELISA technique.

Results: Mean cIMT was higher in diabetics than controls ($P = 0.01$). Moreover, it was higher in diabetics with positive microalbuminuria compared to normo-albuminuric ($P = 0.018$). cIMT was found to positively correlate with: age in diabetics ($P = 0.000$), body mass index ($P = 0.000$). Mean aggregate cIMT positively correlated with duration of diabetes, systolic blood pressure SDS as well as Hb A_1c and correlated negatively with HDL ($P < 0.01$). ADAMTS-13 serum levels were significantly lower in diabetics compared to controls with the lowest values in complicated patients.Mean ADAMTS-13 levels were negatively correlated with ACR, mean CIMT, HbA1c and mean random blood glucose, ($P < 0.001$). ADAMTS-13 levels were negatively correlated with TG, TC, high sensitivity CRP and positively with LDL ($P < 0.01$). Multiregression analysis showed that UACR, and hs-CRP were independently related to ADAMTS 13 levels ($P < 0.05$).ADAMTS 13 levels were related to severity of MVCs as patients with combined MVCs had significantly lower levels compared to patients with single MVCs.

Conclusion: ADMTS13 levels were eleveted and young type1 diabetics and related to metabolic control, dyslipidemia, CIMT as well as severity of MVCs.

P-515-101

Adolescent type 1 diabetes cardio-renal intervention trial (AdDIT): differences in baseline retinal vascular geometry characteristics

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Aim: To study the baseline retinopathy status and retinal vascular geometry (RVG) in participants from AdDIT

Methods: Digital retinal photographs obtained from certified centres in Australia, Canada & UK were deidentified and securely transferred to RetVIC for RVG grading by a single grader, blinded to ACR tertiles, using a semi-automated computer program: Singapore-I-Vessel-Assessment-Tool. RVG measures examined: central retinal arteriolar (CRAE) & venular (CRVE) calibers,

Length: Diameter-ratio (LDR), Simple & Curvature Tortuosity (ST & CT respectively), and branching angles (BA). Urinary ACR tertiles were adjusted for age, gender and duration. Upper tertile=''High-risk''; Lower tertile=''Low-risk''.

Results: Baseline data and retinal vascular calibres were available for 337 adolescents (137Low-risk and 210High-risk; 51%Male). The proportion of participants with retinopathy was not different between risk groups (3% vs 4%). The high risk group had shorter diabetes duration (P = 0.01) and higher diastolic blood pressure (P = 0.05). HbA1c did not differ significantly (P = 0.3). Complete RVG was available in 227 participants (143High-risk, 85Low-risk; 47%Male). The High-risk group had narrower arteriolar BAs (83.1° vs 86.1°, P = 0.02) and no other significant RVG differences. Females had significantly wider CRAE (P = 0.001), lower arteriolar LDR (P = 0.04), greater ST (P = 0.05), CT (P = 0.02) and greater venular CT (P = 0.04) than males.

Conclusion: Baseline differences in retinal vascular geometry were evident between high- and low-risk groups which may herald early microvascular dysfunction. There was significant gender dimorphism in retinal vascular geometry with associated differences in ACR and glycaemic control. Retinal vascular geometry may be a useful marker for future risk of diabetes complications.

Table 1: Baseline Characteristics and Retinal Vasc.

	Low Risk n=137	High Risk n=210	P	Male	Female	P
Age(yrs)	14.9 [2.2] 8.0 [5.8] 71/127 (56) 8.3 (1.3) 64.7 (13.3) 0.73 (0.19) 160.4 (15.0) 237.0 (21.4) 0.68 (0.06) 15.2 (5.9) 111.7 (2.8) 0.99 (0.31) 86.1 (8.4) 12.7 (4.6) 109.7 (1.4) 0.93 (0.39) 81.1 (9.2)	14.5 [2.6] 5.9 [4.9] 101/210(48) 8.5(1.3) 67.0(14.4) 1.70[0.92] 162.9 (13.6) 239.4 (21.2) 0.68 (0.05) 15.6 (6.4) 111.5 (2.8) 1.00 (0.24) 83.1 (8.7) 13.4 (5.7) 109.6 (1.3) 0.94 (0.19) 80.6 (8.5)	0.2 0.01 0.1 0.3 0.05 <0.001 0.1 0.3 0.5 0.7 0.7 0.7 0.02 0.4 0.8 0.8 0.7	14.8[2.6] 6.2 [5.6] 8.1(1.3) 65(8.0) 0.73[0.19] 161.5(13.2) 237.9(19.8) 0.68(0.05) 16.3 (6.1) 110.8[3.0] 0.95(0.27) 84.1(8.4) 13.0 (6.3) 111.3(1.4) 0.90(0.19) 80.1(9.0)	14.5[2.4] 7.0[5.3] 8.7(1.3) 67(8.7) 1.70[0.92] 166.1(12.7) 239.9(20.7) 0.69(0.05) 14.6 (6.4) 111.7[3.0] 1.00 (0.27) 84.8(8.7) 12.6(4.8) 111.8(1.3) 0.97(0.34) 81.4(8.5)	0.2 0.2 <0.001 0.04 <0.001 0.001 0.4 0.02 0.04 0.046 0.02 0.5 0.6 0.2 0.04 0.3

[Table 1. Baseline Characteristics and Retinal Vasc]

P-516-102

Acute mesenteric ischaemia: a thrombotic complication of diabetic ketoacidosis?

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Introduction: Increasing evidence is emerging that demonstrates the increased prothrombotic risk associated with DKA. We present the case of a child who developed multiple complications which we believe can be explained by his hypercoaguable state.

Case history: A 14 month old male was admitted in DKA at first diabetic presentation, complicated by cardiovascular shock. Initial blood tests showed blood glucose 80 mmol/l, blood ketones 5.9 mmol/l and venous pH 7.2. He initially responded well to fluid replacement and insulin therapy according to BSPED guidelines, but subsequently developed abdominal distension and fulminant hyperkalaemia (K^+ 10.3 mmol/l). Following stabilisation, laparotomy was performed with excision of 106 cm of necrotic jejunum and formation of a duodenal-ileal anastomosis. Post-operative course was complicated by multi-organ failure, development of arterial and venous femoral vasculature thrombosis, high stoma losses and difficult diabetes control. Despite this the patient survived and was eventually able to be discharged home following reversal of his ileostomy.

Conclusions: Acute mesenteric ischaemia (AMI) is a rare complication of DKA. While there are a number of cases described in the adolescent and adult population with long term IDDM, only two cases have previously been described in the literature of children developing AMI at first diabetic presentation. These authors differ in their conclusion as to whether non-occlusive ischaemia or thrombotic causes are responsible for AMI in DKA. We believe our report puts a strong case for a thrombotic aetiology, given the level of hyperosmolarity present in our patient and, more significantly, the concurrent development of arterial and venous thromboses. This also provides a platform for discussion of the recommendation in the latest BSPED guideline to give prophylactic anticoagulation in DKA. Furthermore we highlight the diagnosis and management of a rare aspect of DKA which nevertheless has important lessons for the clinician due to its associated morbidity and mortality.

P-38-103

Urinary C-peptide/creatinine ratio as a marker for endogenous insulin secretion: relation to microvascular complications

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Background: C-peptide measurement in blood or 24-hour urine samples provides useful information regarding endogenous insulin secretions.

Objectives: To evaluate urinary C peptide/creatinine ratio (UCPCR) as a marker of endogenous insulin secretion and its relation to disease duration and complications in patients with type 1 diabetes mellitus (T1DM).

Patients and methods: Ninety patients with T1DM (46 males and 44 females) and thirty age and sex matched controls were included. Patients were divided into 3 groups (30 patients each) according to disease duration; group I: ≥5 years; group II: <5 years and group III: at diagnosis. They were further subdivided according to the presence of microvascular complications into; complicated (20 patients) and none complicated (70 patients) groups. Data collected regarding; age, sex, disease duration, diabetic complications, anthropometry and tanner score. Laboratory investigations included; mean HbA1C %, urinary albumin excretion (UAE), blood C-peptide, second void UCPCR. 24 hour-urinary C-peptide was done in controls to make sure of comparable results with UCPCR.

Results: Blood C-peptide and UCPCR were positively correlated in patients, controls and among different studied groups with significantly higher levels (1.5–2.5 ng/ml and 29.7–29.9 respectively) in controls (P < 0.001) and lower levels (0.6–0.8 ng/ml and 4–15.3 respectively) among group I (P < 0.05) and among complicated group (0.2–0.6 ng/ml and 5–11 respectively) (P < 0.001). There was a significant positive correlation between both blood C-peptide and UCPCR with age, age at diagnosis and BMI percentiles and a significant negative correlation with disease duration, frequency of hypoglycemia and mean HbA1c. No significant difference in both blood C-peptide and UCPCR in relation to sex or pubertal stage.

Conclusion: UCPCR can be used as a sensitive and reliable marker of endogenous insulin secretion, being the least with prolonged duration and among complicated group.

P-122-104

Metabolic control in diabetes during the first year after diagnosis in childhood and its importance for metabolic control, risk of retinopathy and albuminuria during the first year as an adult

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Objectives: By using information from the two quality registries for diabetes in Sweden we investigated if the metabolic control measured by HbA1c during month 3–15 after diagnosis in childhood has any importance for metabolic control and the risk for late complications during the first years as an adult.
Methods: Sweden has two quality registers for diabetes, one for children SWEDIABKIDS (SWE) and one for adults, NDR. During the years up to year 2010 have 4854 patients with type 1 diabetes moved from SWE to NDR. Of these patients we have information from 1543 patients HbA1c- values during month 3–15 after diagnosis. Most of the patients have been within NDR up to 2–4 years. The patents had a mean number of 19.5 visits within SWE and 4 visits within NDR. The mean age in NDR is 21 ± 2.3, range 18–29 years of age.
Results: Patients with a high meanHbA1c (≥70 mmol/mol) month 3–15 after diagnosis had years later in NDR a significantly higher mean HbA1c than patients with a low mean HbA1c value (≤50 mmol/mol), 78.8 ± 17 and 61.1 ± 14 mmol/mol, respectively ($P < 0.001$). The patients in the high group had also a lower physical activity and smoked more as adults, 36% smokers compared to 14%, $P < 0.01$. Patients with macroalbuminuria in NDR had significantly higher mean HbA1c month 3–15 after diagnosis than patients without, 65.1 ± 17 and 53.1 ± 14 mmol/mol ($P < 0.001$). This pattern was also seen for patients with retinopathy. Patients with complications had also longer duration of the disease.
Conclusions: A poor metabolic control (high HbA1c) during month 3–15 after diagnosis in childhood is a risk factor for poor metabolic control and risk for albuminuria and retinopathy during the first years as an adult.

P-177-105

Evaluation of the outcomes of application of ISPAD versus ADA guidelines in management of diabetic ketoacidosis in type 1 diabetic children

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Diabetic ketoacodosis (DKA) is a serious complication of diabetes mellitus, especially type 1, and its secondary consequences account for a large proportion of diabetes-related hospitalizations and mortality in children with type 1 diabetes.
Aim: The aim of this study was to compare between the outcomes of application of ISPAD (International Society of Pediatric & Adolescence Diabetes) versus ADA, (American Diabetes Association) guidelines for management of diabetic ketoacodosis in type 1 diabetic children attending the National Institute of Diabetes & endocrinology in Cairo, Egypt (NIDE).
Subjects and methods: Each protocol had been applied on 100 diabetic children with DKA with no significant difference between both groups as regarding, age, sex, acidity represented by ph. and serum bicarbonate and anion gap or coma score.
Results: The results showed that there was no statistical difference as regarding all outcome results the morbidity or mortality results. While the results of the change in potassium was better in ISPAD protocol. The Net results showed that there is no great difference between both groups as regarding the occurrence of the complications.
Discussion: As there was no significant differences between both guidelines, It could be recommended to apply any of the ISPAD protocol for management of DKA in type 1 diabetic children. But, the ISPAD protocol, as it will give better results as regarding the decrease of potassium levels, although it will take longer time for cure from DKA. It will be more beneficial to delay the insulin therapy for 1 hour after giving the intravenous fluid therapy as had been recommended by the ISPAD guidelines.

P-203-106

Retinal vascular geometry in adolescents with type 1 diabetes: a pilot study

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Objectives: To characterize retinal vascular geometry in 31 adolescents with type 1 diabetes (T1D). We hypothesized that retinal vascular geometry measures would correlate with diabetic retinopathy risk factors and would differ in subjects with incipient retinopathy (DR^+) compared to those without retinopathy (DR^-).
Methods: Clinical examination and 2-field 60° retinal photography completed within 6 months of a research visit were used to assess retinopathy status. Retinal vascular geometry was quantified using the Singapore I Vessel Assessment (SIVA) program. Measurements included arteriole and venular caliber (CRAE & CRVE), junctional exponent (JE), tortuosity (TORT), branching angles, fractals (Df) and length-to-diameter ratio (LDR). Correlations were performed between these measures and A1c, BP, and lipids. Next, SIVA measures were compared between 14 cases with DR^+ (microanuerysm or greater) and 17 DR^- age, sex and T1D duration similar subjects.
Results: Subjects were age 15.4 ± 2.0 years, 52% male, 87% non-Hispanic White, A1c 9.1 ± 1.5%, and T1D duration 10.2 ± 2.4 years. The following retinal measures were correlated ($P < 0.05$) with retinopathy risk factors: CRAE/CRVE ratio with A1c ($r = -0.51$), duration ($r = -0.37$), HDL-c ($r = 0.36$), and TG ($r = -0.42$); arteriolar JE with A1c ($r = -0.41$) and duration ($r = -0.40$); venular JE with DBP ($r = 0.49$); venular TORT ($r = 0.38$) with A1c; Df with TC ($r = -0.37$), HDL-c ($r = -0.37$), and SBP ($r = -0.39$). Subjects in the DR+ group had smaller CRAE/CRVE ratio (0.71 ± 0.06 v 0.66 ± 0.06, $P = 0.04$) and venular LDR (12.9 ± 5.7 vs 8.3 ± 7.4, $P = 0.06$, though not significant).
Conclusions: In this pilot study in T1D adolescents, retinal vascular geometry measures were correlated with risk factors for retinopathy. Patients with retinopathy had significantly smaller vessel caliber ratio even in this small sample. Further study is required to determine the role of retinal vascular geometry in screening for early T1D vascular complications.

P-244-107

Treatment outcome of hypoglycemia in children younger than seven years of age with T1DM

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Objective: To investigate treatment outcome in hypoglycemia in children younger than seven years of age with T1DM.

Methods: Twenty-three children (12 girls, 18 on CSII; 5 on MDI, mean age 4.5 years, mean diabetes duration 2.0 years, HbA1c 58.8 mmol/mol, 9.74 SMBG/day) used CGMS Gold (Medtronic). The sensor system was applied and calibrated according to instructions from the manufacturer. The monitor was blinded to the family and diabetes team. Data from p-glucose meters were uploaded via Diasend (Aidera). Data on treatment of hypoglycemia were collected via a logbook. Families were asked to provide data from two separate weeks, one in autumn and one in spring. Hypoglycemia was defined as plasma glucose ≤3.9 mmol/l and hyperglycemia as plasma glucose ≥10 mmol/l.

Results: Mean CGM registration time was 204 hours, with a total of 4689 hours available for analysis. The frequency of hypoglycemia in CGM data was 2.1/24 hours. Data on detection and treatment were available for 387 events.

Plasma glucose was higher 60 and 120 minutes after the hypoglycemic event if it was treated with an ordinary meal instead of simple carbohydrates (7.1 vs 5.8 mmol/l and 9.8 vs 7.2 mmol/l, respectively) ($P < 0.05$).

Conclusions: Detection and treatment is important to restore normoglycemia and to prevent early relapse in hypoglycemia. Most hypoglycemia is efficiently treated when detected. To treat hypoglycemia with an ordinary meal is associated with a higher risk of overtreatment than treatment with simple carbohydrates.

Table: Treatment outcome.

	Treated within 30 min (n = 87)	Not treated within 30 min (n = 300)	Significance
Normoglycemic after 30 minutes	75%	44%	$P < 0.05$
Overtreated, hyperglycemic after 60 minutes	18%	2.7%	$P < 0.01$
Relapse of hypoglycemia within 3 hours	33%	51%	$P = 0.01$

P-262-108

NGAL, GDF-15 and YKL-40: early biomarkers of cardio-renal disease in type 1 diabetes

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Objectives: Among type 1 diabetic (T1D) patients, 25% develop diabetic nephropathy (DN). In this study we aimed to explore the use of new biomarkers of cardio-renal injury, such as human cartilage glycoprotein 39 (YKL-40), growth/differentiation factor-15 (GDF-15) and neutrophil gelatinase-associated lipocalin (NGAL) in patients with T1D.

Methods: 65 T1D patients, aged 5–22, were included in the study. Along with standard blood and urine chemistry, serum (s) and urine (u) NGAL levels, as well as serum levels of GDF-15 and YKL-40 were measured by means of immunoenzymatic assays. GFR was calculated with the Schwartz formula.

Results: The GDF-15 was positively correlated with sCreatinine (sCr)($r = 0.43$, $P = 0.01$) and negatively correlated with both YKL-40 and sNGAL ($r = 0.29$, $P = 0.02$ and $r = 0.26$, $P = 0.04$, respectively). Regression analysis revealed a positive correlation of patients' sNGAL with their YKL-40 ($r = 0.38$, $P < 0.001$). YKL-40 positively correlated with both systolic and diastolic arterial pressure (SAP/DAP) ($r = 0.36$, $P = 0.008$ and $r = 0.37$, $P = 0.006$, respectively). uNGAL positively correlated with DAP($r = 0.01$, $P = 0.01$). No significant correlations between levels of sNGAL, YKL-40, GDF-15, uNGAL with microalbuminuria were found. UNGAL and YKL-40 are also correlated positively with Tanner stage of breast in females ($r = 0.37$, $P = 0.04$ and $r = 0.36$, $P = 0.03$ respectively).

Conclusion: GDF-15 positively correlated with sCr suggesting that it may be used as early marker of DN. The positive correlation of NGAL and YKL-40 with AP further suggests that they may be early markers of cardiovascular morbidity in T1D. These findings imply that early assessment of these markers may unmask the initial endothelial dysfunction in T1D patients before overt microalbuminuria and renal impairment supervenes.

P-473-109

The influence of metabolic disorders in children with diabetes mellitus type 1 on changes of QT interval

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Objectives: To evaluate values of intervals QT and QTc in children with Diabetes Mellitus type 1 (DM1) and to reveal interrelation of the given changes with the duration of disease, age, sex, indices of metabolic control.

Methods: QT and QTc were evaluated on ECG in 178 children with DM1 (middle age 13.44 ± 0.29 years, duration of disease 5.72 ± 0.28 years) and in 60 sex- and age-matched healthy children.

Results: Increases of values of intervals QT and QTc are characteristic to children with DM1 in comparison with control group (364.56 ± 2.65 ms and 421.39 ± 3.1 ms, 352.97 ± 15.1 ms and 392.73 ± 13.0 ms respectively, $P < 0.0015$). It is established that values of QTc in girls with DM1 are higher than in boys (428.07 ± 4.51 ms vs 413.6 ± 4.08 ms, $P < 0.0025$). 17.71% of girls and 13.41% of boys with DM1 have autoimmune thyroiditis (the percent of children with values of QTc>440 ms is high in this group). Levels of thyroid-stimulating hormone (TSH) and thyroperoxidase antibodies (Anti-TPO) are different before and after manifestation of Diabetes Mellitus type 1 (4.21 ± 0.44 mIU/ml and 83.13 ± 13.45 IU/ml, 5.52 ± 1.06 mIU/ml and 251.62 ± 32.66 IU/ml respectively, $P < 0.0002$). At the same time values of HbAc1, are higher in boys than in girls (10.4 ± 0.3% and 9.35 ± 0.2% respectively, $P < 0.002$). The difference in pulse rate between girls and boys is insignificant for the group studied. Connection of QTc with age ($r = 0.338$, $P < 0.00001$) and level of HbA, ($r = 0.37$, $P < 0.0001$) was established. Feedback connection of QT with pulse rate was revealed ($r = -0.48$, $P < 0.005$).

Conclusions: The increase of QT and QTc is noticed in children with DM1. Age, level of glycemie and pulse rate are the factors defining values of QTc. In girls QTc has higher values more often than in boys. Intervals QTc >440 ms are found more often in children with DMI and autoimmune thyroiditis.

Poster Tour 4 - Diabetes Acute and Chronic Complications

P-283-066

Incidence and correlates of severe hypoglycemia in children and adolescents with T1DM

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Objectives: To evaluate the incidence and correlates of severe hypoglycemia (SH) in a large sample of children and adolescents with T1DM.

Methods: Retrospective study conducted in 29 diabetes centers in Italy. The incidence of SH episodes requiring hospitalization or the administration of glucagon in the previous 12 months was assessed through a questionnaire administered by health care professionals to parents of patients aged between 0 and 18 years. Information on a large array of patients and family characteristics was also collected. Incidence rates are expressed as number of events/100 patients/year (py). The risk of SH events was estimated through logistic regression analysis, adjusted for patient gender, age, diabetes duration, and insulin dose. Results are expressed as odds ratios (ORs) with their 95% confidence intervals (95% CIs).

Results: Overall, 2025 consecutive patients were included (mean age 12.4 ± 3.8 years; 53% males; mean diabetes duration 5.6 ± 3.5 years; 21.1% treated with CSII; mean Hba1c levels 7.9 ± 1.1). The incidence of SH was of 7.7 events/100 py (13.3, 9.9, 5.8 and 7.8/100 py in those aged <5, 5–9, 10–14, and 15–18 years, respectively). The risk of SH was more than twice in individuals treated with NPH insulin as compared with insulin glargine (OR = 2.4; 95%CI 0.9–6.2) and in those treated with short-acting insulin analogues as compared with regular human insulin (OR = 2.5; 95%CI 1.2–5.3). Patients treated with pre-mix insulin schemes or MDI did not show an increased risk of SH as compared with those treated with CSII. Among parents' characteristics, mother's age was inversely associated with the risk of SH (OR = 0.95; 95%CI 0.92–0.99).

Conclusions: Despite the advances in insulin therapy, the risk of SH is still elevated among children and adolescents with T1DM, and is more associated with treatment modalities than with patient and family characteristics.

P-332-067

Frequency and risk factors of ketoacidosis in children with newly diagnosed type 1 diabetes mellitus

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Objective: To evaluate the frequency and potential factors influencing the severity of presentation in children with newly onset type 1 diabetes referred to a large tertiary endocrine and diabetes care center.

Methods: 335 children (172 M, 163 F) with newly diagnosed diabetes at a median age of 8.4 years (range 3 months to 17.5 years) between 2000 December and 2012 January were evaluated. Birth weight, family history, parental education, pubertal status and laboratory data were reviewed. Children with diabetic ketoacidosis (DKA) were evaluated in 3 groups as severe (pH <7.1), moderate (pH 7.1–7.2) and mild (pH 7.2–7.3) DKA.

Results: Mean serum glucose was 439 ± 170 mg/dl (range 129–1330), venous pH was 7.26 ± 0.14 (range 6.8–7.4), venous bicarbonate was 15.7 ± 6.7 meq/l and HbA1c was 11.3 ± 2.2 (range 6.9–19.2). The frequency of DKA was 147/335 (43.9%). The ratio was 44/80 (55%), 58/121 (47.9%) and 45/134 (33.5%) in children <5 years, between 5–10 years and >10 years, respectively. Age correlated with blood pH(r = 0.18, P = 0.033) and serum bicarbonate levels (r = 0.19, P = 0.022). Serum glucose levels correlated with level of maternal education (r = -0.15, P = 0.03). Severe DKA was observed in 18/44 (41%), 17/58 (29.3%) and 9/45 (20%) of the children in the respective age ranges. Children <5 years and 5–10 years had significantly higher risk of having severe DKA than others [OR: 2.4, 95% CI: 1.35–4.22, P = 0.003]. Age <5 years (P = 0.007), positivity of anti-GAD antibodies (P = 0.018), prepubertal status (P = 0.002), lack of family history of diabetes (P = 0.033) indicated significantly high risk of DKA. Subgroup analysis of children with DKA revealed that the degree severity of DKA correlated significantly with maternal education level (r = -0.459, P = 0.012).

Conclusions: Younger age, lack of family history of T1DM and presence of anti- GAD antibodies were associated with increased risk of DKA, and high level of maternal education was a negative risk factor for severe DKA.

P-357-068

Glycoalbumin/ HbA1c ratio as a glycation index for complications in Japanese children and adolescence with type 1 diabetes: influence of NGSP and IFCC numbers as HbA1c value

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Objective: Consistency of Glycoalbumin/HbA1c (GA/A1C) ratio has been observed over time in a type 1 diabetes patient, whereas the ratio has been used in the assessment of either improving or worsening glycemia within a past few weeks. This study aims to clarify the consistency of GA/A1C ratio over time on the basis of Glycation (G) -gap, the discrepancy in relative amounts of glycation, and to suggest the future clinical application.

Methods: Simultaneously measured GA and HbA1c were examined every 4 months over 3 years in 433 T1DM patients in the 3rd cohort of multi-center collaboration study, JSGIT. The G-gap was calculated as G-gap = HbA1c minus the standardized GA-derived HbA1c in each term. Both NGSP and IFCC HbA1c numbers were used to test the influence on GA/A1C ratio.

Results: GA/A1C ratios in each patient remained relatively consistent for 3 years with coefficient variation less than 10%.

The G-gap did not differ in absolute or relative terms and within subject variability. GA/A1C ratios were highly correlated with G-gaps in each term ($R^2 > 0.64$, $P < 0.0001$). The mean values of GA/A1C ratios showed near normal distribution in this cohort, whereas GA/A1C ratio was affected by HbA1c value itself. While GA/A1C ratios showed a small but significant positive correlation with HbA1c expressed by NGSP numbers (A1C-N), respective GA/A1C ratios showed weak and negative correlation with HbA1c expressed by IFCC numbers (A1C-SI).
Conclusions: GA/A1C ratios appear consistent over time on the basis of G-gap. Thus, the individual consistency of GA/A1C ratio must be taken into consideration as a glycation index for various diabetic complications. The intrinsic GA/A1C ratio in each patient would be expressed as a Z-score determined by the respective mean value in a specified group or cohort such as Japanese T1DM patients in this study. We should note whether a Z-score of GA/A1C ratio is calculated by A1C-N or A1C-SI, since GA/A1C ratio is affected by HbA1c value itself.

P-510-069

Lowering effect of valsartan on seum levels of Fetuin-A in type 1 diabetes

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Background: Fetuin-A is a protein that plays several functions in human physiology and pathophysiology. The role of Fetuin-A in type 1 diabetes (T1D) has been less studied. Herein, we have studied the serum levels of Fetuin- in T1D patients with microalbuminuria. Furthermore, the blocking effect of renin-angiotensin-aldosteron system (RAS) on serum levels of Fetuin-A was assessed.
Methods and participants: From January 2010 to May 2011, 32 eligible T1D patients with confirmed microalbuminuria were included in this cross sectional study in Isfahan, Iran. Serum Fetuin-A levels before and 8-weeks after valsartan administration were measured. In addition, serum lipid profile, fasting blood sugar (FBS), creatinine, hemoglobin A1C, and urine microalbumin were determined.
Results: The mean age of participants was 21.65 ± 0.38 years, with the median value of 19 years. Before valsartan administration, mean values of Fetuin-A were not significantly different between males and females (64.2208 ± 1.77426 vs 61.3931 ± 3.35136 ng/ml, respectively; $P > 0.05$). After valsartan administration, serum levels of Fetuin-A and urine microalbumin/Cr decreased significantly ($P < 0.05$). Nonetheless, a negative correlation was observed between serum Fetuin-A level after valsartan administration and serum LDL level ($P = 0.007$, $r = -0.507$).
Conclusion: Valsartan (ARBs) administration concomitantly decreases Fetuin-A levels and urine microalbumin levels.

P-18-070

Glycemic control and acute complications in children and adolescents with type 1 diabetes at Kilimanjaro Christian Medical Centre in Moshi, Tanzania

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Objective: The purpose of this study was to assess glycemic control and acute complications in children and adolescents in Tanzania.
Reseach design and methods: There are an estimated 1000 children with diabetes in Tanzania. Recently, the first two pediatric endocrinologists, trained in the ESPE/ISPAD program in Nairobi, entered practice at the Kilimanjaro Christian Medical Centre. A longitudinal study was conducted over a 6 month period, to assess baseline diabetes control and the impact of a diabetes education program. Eighty-one children and adolescents age 3–19 years were enrolled. All were on split-dose Insulatard (NPH) and Actrapid (soluble, regular) insulin, and were given enough test strips to test 3x/week. Children were seen in clinic an average of six times over 6 months and received 3 hours of diabetes education. A structured questionnaire was used for evaluating social demographic data and prevalence of acute complications.
Results: Despite regular clinic attendance, diabetes education and adequate provision of insulin, HbA1c levels did not improve. Four children (5%) had HbA1c 7.5%, 22 (28%) HbA1c 7.5–10%, 9 (24%) HbA1c 11–12.5%, and 36 (44%) HbA1c >12.5%. During the 6 month study period, there was a substantial reduction of severe hypoglycemia (had to be helped by others), with 17% of subjects experiencing this acute complication compared to 52% in the 6 months prior to study enrollment. Six children were admitted in DKA during the study compared to three admissions the previous 6 months. Twenty six children (36%) reported missing more than six doses of insulin for variable reasons.
Conclusion: Diabetes education significantly reduced the risk of severe hypoglycemia, but better glycemic control of diabetes was not attained. Further study is needed to explore factors to improve glycemic control including better ability to measure blood glucose levels or perhaps different insulin regimens.

P-65-071

The effect of CaNa2-EDTA on zinc, carbohydrate metabolism and glutamic oxalic, glutamic pyruvic aminotransferases (GOT, GPT) and alkaline phosphatase activities in experimental diabetes

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To investigate the effect of CaNa2-EDTA and experimental diabetes (IDDM) on zinc and carbohydrate metabolism and the activities of GOT, GPT and alkaline phosphates. Forty male wealing normal albino (Wistar) rats of 8 weeks of age were fed with a basal diet. Twenty rats ($n = 20$) were then intraperitoneally injected with alloxan to induce diabetes. Then after one week ten rats from each group ($n = 20$) were administrated intraperitoneally with CaNa2-EDTA for further three weeks. Body weight gain and food intake were recorded regularly. On day 21 after an over night fasting, animals were killed and blood glucose, serum zinc, femur and pancreatic zinc concentrations, liver glycogen contents, serum glutamic oxalic transaminase (GOT), serum glutamic pyruvic transaminase (GPT) and serum alkaline phosphatase were determined. Diabetic rats given CaNa2-EDTA or not had a low body weight gain, high total food intake (hyperphagia), low liver glycogen contents and low serum and pancreatic zinc concentrations compared to normal ones. The administration of CaNa2-EDTA significantly altered the body weight gain, food intake and serum zinc concentration of either diabetic or non-diabetic animals. Both diabetic and non-diabetic rats given CaNa2-EDTA had higher blood glucose than their control counterparts. Liver glycogen was also found to be higher in CaNa2-EDTA non-diabetic rats than their controls. In alloxan diabetes, serum GOT and GPT were significantly increased compared to normal rats, while the level of serum alkaline phosphatase was decreased. The

administration of CaNa2-EDTA led to increasing of GOT and GPT, and decreasing serum alkaline phosphatase. To conclude, the present study demonstrates that CaNa2-EDTA had an effect on body weight gain, glucose utilization and serum zinc. In addition CaNa2-EDTA has affected the activities of GOT, GPT and alkaline phosphatase. Therefore it was appeared that CaNa2-EDTA resulted in the development of severe diabetes.

P-112-072

Prevalence of acute complications, renal disease, and cardiovascular risk factors (CVrf) in youth with type 1 diabetes (T1D) participating in the T1D Exchange Clinic Registry

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Objective: To describe the prevalence of acute and chronic complications in youth with T1D <18 years of age participating in the T1D Exchange Clinic Registry at 60 diabetes centers in the US.
Methods: The proportion of patients with ≥1 episode of severe hypoglycemia (SH, seizure or coma) or DKA in the prior year and with microalbuminuria (MICRO) and macroalbuminuria (MACRO) were analyzed by age group and disease duration. CVrfs included overweight/obesity (OW/OB), dyslipidemia (LIPID), and hypertension (HTN).
Results: In 12 843 youth, 52% were male, 47% used insulin pumps, mean age was 11.4 ± 3.8 years, T1D duration was 4.5 ± 3.8 years; mean A1c was 8.5 ± 1.6% and only 25% met ISPAD A1c goal of <7.5%. The percent of patients with SH was similar in pre-teens and teens (Table); whereas a greater proportion of teens with longer duration had DKA, OW/OB, abnormal lipids and HTN. Moreover, MICRO/MACRO was increased nearly 2-fold in the teens. 32% of pre-teens and 39% of teens had ≥1 CVrf.
Conclusions: SH and DKA remain all too common complications of treatment and over 1/3 of youth with T1D were OW/OB or had another CVrf. Even in patients with long duration of T1D, pre-teens appeared to be protected against the development of early diabetic nephropathy. Future efforts to assess the predictors of complications and current management of these youth may better inform treatment gaps and opportunities to prevent future complications.

	SH	DKA	OW/OB	LIPID	HTN	MICRO/ MACRO	A1c ≥7.5%
Age <13 years							
Duration <5 yrs	4%	6%	32%	0.8%	0.1%	1.4%	71%
Duration 5-<10 yrs	6%	8%	32%	2.8%	0.3%	2.7%	78%
Duration ≥10 yrs	6%	8%	23%	3.2%	0.0%	4.1%	85%
Age 13-<18 years							
Duration <5 yrs	3%	7%	34%	1.2%	1.4%	3.8%	67%
Duration 5-<10 yrs	7%	13%	43%	3.5%	1.4%	5.0%	83%
Duration ≥10 yrs	7%	11%	38%	4.1%	1.9%	6.1%	83%

[Table]

P-323-073

Bone turnover markers in children and adolescents with type 1 diabetes mellitus

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Objectives: The aim is to examine the levels of some markers of bone metabolism (ß - beta cross laps and bone-specific alkaline phosphatase) and IGF-1 in children with type 1 diabetes in order to determine if there is any relationship between the examined markers and the glycemic control (HbA1c) and/or the duration of the disease.
Methods: A cross-sectional study of 53 patients with type 1 diabetes (29 males and 24 females) aged 11.38 ± 4.03 years and duration of the disease 6.31 years (0 to 16 years). The mean level of HbA1c- 10.25 ± 2.06%. We have divided the patients in 2 groups according to HbA1c level: <9%-favorable control (n = 18) and ≥9% -poor control (n = 35) and into 4 groups according to disease evolution: newly diagnosed and with duration of diabetes <5 years, 5–10 years and >10 years. Serum levels of Bone Specific Alkaline Phosphatase (BSAP) and IGF-1 were measured by immunoradiometric assay, beta cross laps - by electrochemiluminescence immunoassay, HbA1c by immunoturbidimetric method. The statistical methods used were variation and regression analysis.
Results: The duration of type 1 diabetes influences the level of BSAP: we found statistically significant differences of the serum levels of BSAP between the subgroups of newly-diagnosed diabetes and that of <5 years duration (t = 3, 11 $P < 0.01$), as well as between the subgroups with diabetes duration <5 years and 5–10 years (t = 2, 11 $P < 0.05$). We also found a negative correlation between the level of HbA1c and BSAP in boys(r = -0.464, $P < 0.01$), but not in girls (r = 0.03, P = 0.866). We did not find any statistically significant difference between the other parameters concerning the level of HbA1c and/or the duration of diabetes.
Conclusions: Our results show an association between BSAP-bone formation marker and diabetes duration. The relationship between BSAP and HbA1c in boys and not in girls could be related to other unknown factors /hormonal/ which need further investigation.

P-410-074

Vitamin D deficiency in children and adolescents with type 1 diabetes

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Objective: To investigate the frequency of vitamin D deficiency in children and adolescents with type 1 diabetes (T1D) and to evaluate demographic and biochemical features of these patients.
Methods: In this retrospective study, 68 children and adolescents with T1D (23 boys and 45 girls) aged 4–21 years were evaluated. Serum 25-hydroxyvitamin D [25(OH)D] was measured. Hemoglobin A1c levels and duration of T1D were also evaluated. Classification of vitamin D status was made according to the American Academy of Pediatrics (AAP)/ LWEPS's recommendations.
Results: Serum 25(OH)D levels revealed vitamin D deficiency or insufficiency in 69% of the patients (insufficiency in 28%, deficiency in 32% and severe deficiency in 9%), 55% of the boys and 45% of the girls. The 25(OH)D status level was normal (sufficient) in 31% of the patients. None had vitamin D excess.

The mean 25(OH)D level of the girls was 17 ng/ml (range: 2–40) and that of the boys was 16.1 ng/ml (range: 2–28). The mean hemoglobin A1c levels and duration of T1D were respectively 9.2% and 6.3 years in patients with normal status level of 25(OH)D, 8.8% and 5.7 years in patients with 25(OH)D deficiency or insufficiency.

Conclusion: The frequency of vitamin D deficiency in T1D children and adolescents is substantial, regardless the sex. In this study the mean hemoglobin A1c levels is independent of the 25(OH)D status level.

P-449-075

Is Mauriac only a syndrome or a spectrum?

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Background & aim: Classic Mauriac Syndrome (MS) is known as a rare condition that seen in poorly controlled type-1 diabetics due to underinsulinization. However, some cases can be presented with isolated hepatomegaly besides the combination of classic symptoms. Thus, we aimed to discuss whether to use Mauriac spectrum term instead of Mauriac syndrome is a better approach.

Methods: We report 8 (5 girls) poorly controlled diabetic patients aged between 7.6–21.3 years, who are within the Mauriac spectrum.

Results: The age of the T1D and MS diagnosis was between 2.3–8.2, 7.5–17 years, respectively. All patients had significant psychosocial problems that interrupt follow-up. Six were underinsulinized, one case was overinsulinized. Four patients had severe short stature, three had delayed puberty. While hepatomegaly was observed in all except one, liver transaminases were elevated in only one case. Cushingoid habitus was seen in seven, although many of them did not have hypercortisolism. HbA1C levels were variable in the range of 13.4–5%.

Conclusions: Although there are a wide variety of insulin regimes in the recent years, MS is not remained in the past. While the classic symptoms had shown in the previously described cases, Mauriac syndrome should be considered as a broad spectrum. Usually high HbA1c levels were observed, but lower HbA1C levels suggesting that recurrent hypoglycemia is likely in some cases. Therefore, low HbA1c levels in cases with poorly controlled T1D do not exclude the diagnosis of Mauriac syndrome/spectrum.

Table: The clinical and laboratory characteristics.

	Age at T1D diagnosis (years)	Age at MS diagnosis (years)	Height SDS	Weight SDS	Delayed puberty	Daily insulin dose u/kg/g	HM	HbA1C (max-min)
case 1	3	7.8	-3.3	-2.4	yes	0.5	4 cm below RCM	13–6.3
case 2	2.3	9	-2.9	-1.9	NA	0.7	5 cm below RCM	9.3–9.9
case 3	6.8	16.9	-3.1	-1.3	yes	0.7	14 cm liver span	9.4–6.8
case 4	6.9	16.5	-1.5	2.2	yes	1	18 cm liver span	12.8–9.1
case 5	8.2	13.2	-1.4	0.3	no	0.68	3 cm below RCM	12.1–8.4
case 6	7.7	16	-0.8	1	no	1	19 cm liver span	13.4–5
case 7	6.9	15.9	-2.69	-0.1	yes	0.85	No HM	8.3–7.9
case 8	4.6	7.5	-1.9	-0.05	no	1.8	6 cm below RCM	10.9

P-277-076

Increased prothrombotic factors in association with poor glycemic control and impaired lipid profile in children and adolescents with type 1 diabetes mellitus

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Objectives: Increased frequency of cardiovascular disease is well established in patients with type 1 diabetes mellitus (T1DM). Although the underlying mechanism is not fully understood, impaired fibrinolysis has been proposed to be related to atherosclerosis. The aim of this study was to

(i) estimate the levels of prothrombotic factors in children and adolescents with T1DM and

(ii) investigate the possible association with athropometric parameters, glycemic control and lipid profile.

Methods: We determined von Willebrand factor-antigen (vWF-Ag), plasminogen activator inhibitor-1-antigen (PAI-1-Ag), fibrinogen (FB) as well as glycosylated hemoglobulin (HBA_{1C}), total cholesterol, triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL), apolipoprotein A1, apolipoprotein B, lipoprotein(a) [Lp(a)] in 155 children and adolescents with T1DM (85 boys, 49 prepubertal, 38 overweight/obese). Statistical analysis was performed using SPSS Statistics 16.0 program.

Results: High age-related levels of PAI-1-Ag, vWF-Ag, and FB were found in 40.0%, 14.8% and 4.5%, respectively in the studied population. Poor glycemic control (HBA_{1C} >7%) was associated with elevated vWF-Ag and FB levels. High PAI-1-Ag levels were associated with high triglycerides, low HDL, low apolipoprotein A1 levels as well as increased body mass index (>85th percentile). Patients having elevated vWF-Ag levels presented

more frequently high total cholesterol, triglycerides, LDL levels, as well as low HDL and apolipoprotein A1 values at statistical significant level. Increased FB levels were associated with high Lp(a) levels.

Conclusions: The elevated prothrombotic factors accompanied by poor glycemic control and impaired lipid profile may contribute to the increased risk for developing cardiovascular disease later in adulthood in patients with TIDM.

Poster Tour 5 - Diabetes Acute and Chronic Complications

P-454-088

Safety results from OCAPI: a European observational cohort study of insulin glulisine-treated children aged 6 to 12 years with type 1 diabetes

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Objectives: Children with type 1 diabetes (T1DM), especially younger children, are at risk of clinically significant hypoglycaemia. OCAPI assessed the safety of insulin glulisine in children with T1DM in a clinical-practice setting.
Methods: This was a 6-month, observational, prospective cohort study of children with T1DM aged 6–12 years on a stable insulin regimen for ≥3 months, for which insulin glulisine was prescribed. Primary endpoint was severe hypoglycaemia incidence in children aged 6–12 (primary objective) and 6–8 years. Secondary endpoints included severe hypoglycaemia incidence in the 6–8 years group, and symptomatic hypoglycaemia, injection site/systemic hypersensitivity reaction, and medication error in both age groups.
Results: Of the 94 patients analysed, 31 were aged 6–8 years. Mean ± SD time from first prescription of insulin to inclusion was 2.3 ± 2.1 and 2.8 ± 2.4 years in the 6–8 and 9–12 years groups, respectively; mean ± SD HbA_{1c} at study end was 8.19 ± 1.46% and 8.29 ± 1.66%, respectively. Basal dose increased during the study period in both groups; short-acting insulin dose increased in the 9–12 years group. Number of daily basal insulin injections did not change. Severe hypoglycaemia occurred in 3 patients (1 in 6–8 years, 2 in 9–12 years group), and incidence for all patients was 6.6 events/100 patients/years (95% CI: 1.4; 19.4). Symptomatic documented hypoglycaemia occurred in 25 (80.6%) and 47 (74.6%) patients in the 6–8 and 9–12 years groups, respectively. Incidence (per 100 patients/years) of symptomatic documented hypoglycaemia was higher in the 6–8 years (7007.2 [6572.5; 7463.2]) vs the 9–12 years group (5717.5 [5456.4; 6342.3]).
Conclusions: Hypoglycaemia was frequent, occurring more in younger children; three severe cases were observed. Overall severe hypoglycaemia rate was lower than reported in the medical literature for this population (9.4–73.0 events/100 patients/years), further supporting the safety of insulin glulisine in this young population.
This study was supported by Sanofi.

P-75-089

Screening of autoimmune thyroid disease in Algerian adolescents with type 1 diabetes mellitus

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Type 1 diabetes mellitus (T1DM) is an auto-immune disease It is associated with other auto-immune endocrine disorders. Auto-immune thyroid disease is one of the most frequent auto-immune diseases associated with it.
Aim of the study: To define the prevalence of thyroid autoimmune disease in West Algerian patients with type 1 diabetes mellitus.
Patients and methods: Blood samples were collected from 100 T1DM patients and 94 patients with T1DM - Coeliac disease, who are followed by the Oran Pediatric Department, Algeria. All patients are more than 15 years at the time of screening were included and whose diagnosis of T1DM was established before the 15 years age. All patients presenting thyroid disease were excluded. Sera of 100 healthy subjects served as controls in each group, the number of the girls was equivalent to the number of the boys. Antithyroperoxidase antibodies (TPO-Ab), was determined by enzyme-linked immunosorbent assay. TSH and FT4 concentrations, thyroid echography were carried in subjects positives for TPO-Ab.
Results: Among of 100 patients with T1DM, 15 (9 girls, 6 boys) had positive TPO-Ab. one patient had evidence of subclinical hypothyroidism. Thyroid echography had revealed 4 goiters. Among 94 patients T1DM-Coeliac disease, 11 (7 girls, 4 boys) had positive TPO-Ab. Three patients had evidence of subclinical hypothyroidism. Thyroid echography had revealed 4 goiters. Among 100 controls, 7 (7 girls) had positive TPO-Ab. one patients had evidence of subclinical hypothyroidism. thyroid echography had revealed 1 goiters.
Conclusions: The prevalence of autoimmune thyroid disease in type 1 diabetic patients (15%) is higher than in the general population (7%). The screening of uto-immune thyroid disease should could be systemic in T1DM patients as the coeliac disease.

P-92-090

Characteristics of diabetes mellitus type 1 cases presenting with ketoacidosis symptoms in Indonesian children

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Background: Diabetic ketoacidosis (DKA) is the most common complication of diabetes mellitus. DKA results from absolute or relative deficiency of circulating insulin and from combined effects of increased counter regulatory hormone levels. This accelerate catabolic state with increased glucose production by liver and kidneys (by glycogenolysis and gluconeogenesis), impair peripheral glucose utilization causing hyperglycemia and hyperosmolality, and increase lipolysis and ketogenesis. Most of Indonesian children with diabetes mellitus (DM) came for the first time with diabetic ketoacidosis.
Objective: To describe the characteristics of diabetes mellitus type 1 cases presenting with ketoacidosis symptoms in Indonesian children.
Methods: A retrospective national survey of Indonesian children was conducted during February 2012-May 2012. Data was collected by using questionnaire, submitted from referral hospitals in Indonesia. Subjects with ketoacidosis complication were included.
Results: Of 759 children with diabetes mellitus in Indonesia, 295 subjects met the criteria. Most children came from Jakarta (39.3%), Palembang (10.1%), Surabaya (8.1%) and Malang (7.7%). Most children were female (62.7%). Most subjects were 10–14 years old (42%) and 0–4 years old (37.6%). From all subjects, 23.7% had family history of type II DM and 4.7% had

family history of type I DM. Most subjects were not obese (94.6%) with body weight are 25.2 ± 11.1 kg and body height are 127.1 ± 24.6 cm. Most subjects had one episode of DKA (84%), but 10.1% and 3% had two or three episodes. Hemoglobin A1c (HbA1c) is 12.1 ± 2.8% from all subjects. Most subjects survived and 5% died from DKA.

Conclusions: Most subjects were female, aged 10–14 years old. Small proportion of subjects had family history of DM. Most subjects had 1 episode of DKA. Most subjects were not obese with HbA1c 12.1 ± 2.8%. Mortality from DKA was 5%.

Keywords: Characteristics, diabetes mellitus, ketoacidosis.

P-118-091

Renal injury biomarkers in children with type 1 diabetes mellitus: preliminary data

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Objective: To cuantificate biomarkers of renal injury, NFAT5 and HIF-1α and NGAL, in type 1 diabetes mellitus(DM-1) children and to compare levels according to metabolic control.

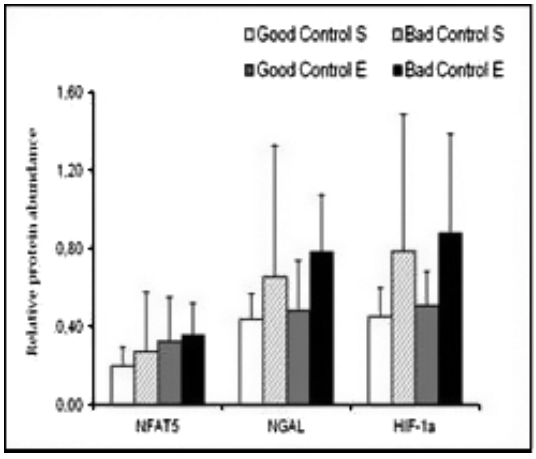

Fig.1. NFAT5, NGAL and HIF-1a in S and E fraction

Table 1 general data and laboratory results.

Group		Good Control	Bad Control
N		4	4
Male /female		3/1	3/1
HbA1c (%)		7,8 + 3,5	11 + 1
Age (years)		14,0 ± 2,7	14,4 ± 0,4
Time DM-1 (years)		6,2 + 2,4	7,5 + 3,5
NFAT5	S1	0,2 + 0,1	0,27 + 0,14
	P2	0,32 + 0,23	0,36 + 0,16
	Total	0,52 + 0,32	0,63 + 0,3
NGAL	S1	0,43 + 0,13	0,65 + 0,42
	P2	0,48 +0,26	0,78 +0,29
	Total	0,91 + 0,32	1,44 + 0,67
HIF-1a	S1	0,45 + 0,15	0,78 + 0,30
	P2	0,5 + 0,18	0,68 + 0,51
	Total	0,95 + 0,32	1,66 + 0,70

Methods: 20 DM-11 children were studied, 2 groups according HbA1c on the last year, couple by age, sex and puberal stage were formed. Preliminar data of 8 DM-1 patiens are presented. Sex, age, time from diagnosis, HbA1c, serum creatinine, microalbuminuria and albuminuria creatininuria ratio were registered. A 5 ml of blood were collected, serum was isolated (centrifugation 4000 g × 10 minutes) and supernatant (S) and exosomes (E) fraction were obtained (ultracentrifuged cell-free serum 38 000 g × 1 hour, 4° C) and treated with lysis buffer. NFAT5, HIF-1α and NGAL concentration were determined in S and E fractions by Western blot. Average and SD were calculated and cluster analysis was done.

Results: Figure 1 Renal injury biomarkers. HIF-1α and NGAL were highly expressed in bad control vs good control group, in S and E. NFAT5 was equally in both in S and E. Each biomarker was lightly increased in E.Cluster anályss show that overall measured biomarkers are grouped according metabolic control en 2 groups.

Conclusions: The present data suggest that the determination of these renal injury biomarkers in children with type 1 diabetes mellitus seems to be a promissory tool for precocious renal involvement in type 1 DM-1 children.

P-293-092

Incidence and correlates of ketoacidosis in children and adolescents with T1DMK

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Objectives: To evaluate the incidence and correlates of hospitalization for ketoacidosis (DKA) in a large sample of children and adolescents with T1DM.

Methods: Retrospective study conducted in 29 diabetes centers in Italy. The incidence of DKA episodes leading to hospitalization in the previous 12 months was assessed through a questionnaire administered by health care professionals to parents of children/adolescents aged between 0 and 18 years. Information on a large array of patients and family characteristics was also collected. Incidence rates are expressed as number of events/100 patients/year (py). The risk of DKA events was estimated through logistic regression analysis, adjusted for patient gender, age, diabetes duration, and insulin dose. Results are expressed as odds ratios (ORs) with their 95% confidence intervals (95% CIs).

Results: Overall, 2025 consecutive patients were included (mean age 12.4 ± 3.8 years; 53% males; mean diabetes duration 5.6 ± 3.5 years; 21.1% treated with CSII; mean Hba1c levels 7.9 ± 1.1). The incidence of DKA was of 2.4 events/100 py (1.3, 1.5, 2.7 and 2.7/100 py in those aged <5, 5–9, 10–14, and 15–18 years, respectively). The risk of DKA increased by 65% for any 1% increase in HbA1c levels (OR = 1.65; 95%CI 1.34–2.03), and was 5 times higher in those treated with short-acting insulin analogues as compared with regular human insulin (OR = 4.8; 95%CI 1.2–20.2). Patients treated with pre-mix insulin schemes or MDI did not show an increased risk of DKA as compared with those treated with CSII. Among parents' characteristics, mother's age (OR = 0.90; 95%CI 0.84–0.95) and level of school education were inversely associated with the risk of DKA.

Conclusions: The risk of DKA is strongly associated with poor metabolic control and insulin therapy modalities. The influence

of mother's characteristics calls for more intensive education to the family of children with T1DM.

P-317-093

Can the cardiovascular risk in type 1 diabetes be detected early?

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Objectives: Type 1 diabetes is a chronic disease that causes persistent injury in vital organs in case of poor glycemic control. Mortality and morbidity due to the coronary artery disease are more common than normal population. This study aimed to investigate the benefits of cardiovascular risk markers in early detection of vascular injury in children and adolescents with type 1 diabetes.

Methods: Eighty-four patients (35 male, 49 female) with type 1 diabetes for five or more years were included. Atherosclerotic risk markers (serum lipid profile, plasminogen activator inhibitor-1 (PAI-1), lipoprotein (a) and homocystein) were investigated. Patients were divided into two groups according to the duration of diabetes. Patients with and without microvascular complications were also compared.

Results: Microvascular complications were present in 14 out of 48 patients (29.1%) of GROUP-1 (duration of diabetes: five to ten years) and in 7 out of 36 patients (19.4%) of GROUP-2 (duration of diabetes: over ten years). HbA1C was significantly higher in patients with complications ($P = 0.017$). Serum triglyceride levels were positive correlated with AST, ALT, cholesterol, LDL and microalbuminuria and negative correlated with HDL. Significant difference in the serum trygliceride levels was present between patients with or without complications ($P = 0.010$). Serum homocystein, lipoprotein (a) and PAI-1 levels were correlated with neither the duration of diabetes nor the presence of microvascular complication.

Conclusion: Evaluation of serum homocystein, lipoprotein (a) and PAI-1 levels in microvascular injury screening of patients with type-1 diabetes do not seem to be meaningful. Optimum glycemic control is the most important issue in cardiovascular risk management. Moreover, evaluation of serum triglyceride, total cholesterol, LDL, HDL and LDL/HDL ratio at least once in a year seem to be the most cost-effective and satisfying approach.

P-342-094

Hyperosmolar hyperglycemic syndrome in children hospitalized in the United States

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Background: Diabetic hyperosmolar hyperglycemic syndrome (HHS) is associated with significant morbidity and mortality. HHS is underdiagnosed in children, as the clinical appearance is similar to shock or diabetic ketoacidosis. Previous studies of HHS in children have been limited to case series or single-institution reviews and described HHS primarily in children with type 2 diabetes mellitus.

Objective: The goal of this study was to estimate the rates and describe the epidemiologic characteristics of HHS among children in the United States.

Methods: We included all hospital discharge records present in the Kids' Inpatient Database– a triennial, nationwide, stratified probability sample of hospital discharges for 1997–2009–with age 0–18 years and a diagnosis of HHS. Using sample weights, we calculated the incidence and population rate of hospitalization with a diagnosis of HHS.

Results: Our sample included 1074 HHS hospitalizations; of these, 42.9% subjects were 16–18 years old, 70.6% had type 1 diabetes (T1D), and 53.0% had major or extreme severity of illness. The population rate for HHS diagnoses for children aged 0–18 years was 2.1 per 1 000 000 children in 1997, rising to 3.2 in 2009. The median length of stay was 2.6 days, 2.7% of hospitalizations ended in death, and median hospital charge was $10 882. When comparing HHS hospitalizations by diabetes type, the proportion with T1D fell steadily with age, from 89.1% among children 0–9 years, to 65.1% in 16–18 year olds. Patients with T1D had a shorter length of stay by 0.9 days, and had a lower median charge by $5311. There was no difference in mortality by diabetes type.

Conclusion: This is a first estimate of national incidence of HHS diagnoses among children. Hospitalizations for a diagnosis of HHS have high morbidity and are increasing since 1997. In contrast to prior reports, we found a substantial percentage of HHS hospitalizations occurred among children with T1D.

P-509-095

The effects of blocking angiotensin receptors on markers of endothelial dysfunction in diabetic nephropathy

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Background: The role of inhibiting the renin-angiotensin system (RAS) in preventing diabetic nephropathy (DN) through improving responsible mechanisms has been discussed widely. However, there is limited evidence about such beneficial effects in early stages of DN. This study aimed to investigate the beneficial effects of angiotensin receptor blockers on markers of endothelial function in patients with early stage of DN.

Methods and materials: This cross sectional study was carried on 32 participants with insulin dependent diabetes mellitus (IDDM) from January 2010 until May 2011 in Isfahan, Iran. The participants were candidate for receiving ARBs or ACEIs to decrease microalbuminuria. The inclusion criteria were as follows: The age of onset of IDDM less than 15 years; normal glomerular filtration rate (GFR); normal blood pressure; normal cardiovascular examination; negative urine culture, receiving no medications except insulin. Microalbuminuria was measured in two fasting urine samples with a sampling interval of at least 1–2 month by ELISA method. Patients with two abnormal results were included. Microalbumin to creatinin ratio equal to or more than 30 mg/gm was considered abnormal. The fasting blood samples to determine serum NO and VCAM were obtained at the time 0 (before starting the study), and after 2 months of receiving the medication. Valsartan tablet (Diovan, angiotensin receptor blocker from Novartis Company) with a dose of 1mg/kg/day up to 80 mg/day in a single dose was administered.

Results: Urine microalbumin to creatinin ratio after Valsartan consumption was lower than microalbumin level before the medication, $P < 0.05$. After valsartan consumption, serum VCAM-1 level reduced and NO level increased significantly, $P < 0.05$.

Conclusion: Angiotensin receptor blocker (valsartan) reduces VCAM-1 and microalbuminuria and increases NO levels in early stages of DN. Thus administration of ARBs might be considered even in early stages of DN.

P-532-096

Correlation between HLA-DQ and late complications in patients with type 1 diabetes mellitus

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Objectives: To explore the possible association between the HLA-DQ genotype and diabetic retinopathy and diabetic nephropathy.
Background: Patients with diabetic microvascular complications despite good metabolic control and familial clustering of diabetic nephropathy seem to indicate a role for genetic factors.
Methods: A retrospective study, approved by the Ethical Committee of 84 diabetic patients. Study population: patients with diabetes mellitus type 1, age at diagnosis <30, disease duration >10 years. A complete data set was obtained for 40 patients. Data:HLA-DQ typing, islet auto-antibodies at diagnosis (ICA, IA-2A, GADA), smoking habits, blood pressure, Hba1c, grade of retinopathy (no retinopathy/non proliferative retinopathy/proliferative retinopathy on dilated fundoscopy with photographs), degree of nephropathy (no albuminuria/microalbuminuria/macroalbuminuria on timed urine collection or albuminuria/creatinuria ratio on urine sample). Statistical analysis: SPSS version 19.0, Mann–Whitney *U* test, Fisher's exact test.Significance level: $P < 0.05$.
Results: Patient characteristics: 19 males/21 females, bloodpressure ($n = 25$): 11 hypertension, smoking ($n = 20$): 6 smokers, diabetic retinopathy ($n = 31$): 4 retinopathy, diabetic nephropathy ($n = 33$): 5 nephropathy. None of the analyzed patients had both retinopathy and nephropathy, disease duration ($n = 40$): 16.4 years (10–45). Hba1c ($n = 34$): mean 8.29% (6.6–11.4). HLA-DQ type ($n = 40$): 23 susceptible/12 neutral/5 protective HLA-DQ type. A correlation was found between disease duration and retinopathy ($P = 0.003$) and GADA-level and nephropathy ($P = 0.021$). A tendency to a higher prevalence of a susceptible HLA-DQ type was observed in patients with either nephropathy of retinopathy.No correlation was found between HLA-DQ type and retinopathy, nor between HLA-DQ type and nephropathy.
Conclusion: No correlation was found between HLA-DQ type and diabetic retinopathy of diabetic nephropathy.Only 9 patients had microvascular complications.

P-10-097

Type 1 diabetes in a known sickle cell anaemia patient: a rare combination

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Background: Sickle cell anaemia is a very common disease condition in Nigeria. Its co-existence with type 1 diabetes mellitus is rare. Only few cases have been reported in literature. Only two children have been reported from Nigeria. The genetic basis for this has not been fully reviewed. Growth failure is a common feature in both pathologies and this could pose a great challenge in management.
Case report: A ten year old girl who presented in October 2011 with 9 year history of recurrent bone pains, yellowness of the eyes and poor growth. She also had a short history of polyphagia, polydipsia and polyuria. Haemoglobin electrophoresis showed SS while a random plasma glucose done at least twice was greater than 200mg/dl. There was no ketosis nor did she have any other adverse complications. She is currently being managed as a case of HbSS patient with T1DM. Her management has been hampered by severe financial constraints.
Conclusion: This report seeks to increase the awareness of this rare co-existence in this environment, as well as to highlight the antecedent challenges in management.

P-61-098

Diabetic cystopathy in Egyptian children and adolescents with type 1 diabetes

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Background: Urinary bladder dysfunction is a major complication of diabetes mellitus and its mechanism has been attributed to autonomic and/or peripheral neuropathy.
Objectives: Evaluation of diabetes mellitus and neuropathy effect on the urinary bladder dynamics in children and adolescents with type 1 diabetes mellitus.
Patients and methods: The study included 80 children and adolescents with type 1 diabetes for at least 5 years; 60 patients with manifestations of autonomic and/or peripheral neuropathy and 20 patients were free of either. We assessed both groups for presence of cystopathy by means of uroflowmetry and cystometry.
Results: All patients with diabetic neuropathy have got abnormal urodynamic test results of variable types and degrees with bladder hypercompliance as the most frequent abnormality. Other urodynamic abnormalities were found in both diabetic patients' groups with no significant difference in frequency.
Conclusions: Diabetic neuropathy might be strongly related to urodynamic abnormalities particularly the bladder hypercompliance. Some diabetic patients may have cystopathy in absence of evident neuropathy. This may be due to undetected neuropathy or diabetes induced myopathy of the detrusor muscle.

Poster Tour 6 - Diabetes Acute and Chronic Complications

P-93-121

Characteristics of diabetes mellitus type 1 cases presenting with ketoacidosis symptoms in Ciptomangunkusumo Hospital

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Background: Diabetic ketoacidosis (DKA) is the most common complication of diabetes mellitus. DKA results from absolute or relative deficiency of circulating insulin and from combined effects of increased counter regulatory hormone levels. This combination can accelerate catabolic state with increased glucose production by liver and kidneys, impair peripheral glucose utilization causing hyperglycemia and hyperosmolality, and increase lipolysis and ketogenesis, resulting in ketonemia and metabolic acidosis. Most of Indonesian children with diabetes mellitus (DM) came for the first time with diabetic ketoacidosis.
Objective: To describe the characteristics of diabetes mellitus type 1 cases presenting with ketoacidosis symptoms in Ciptomangunkusumo Hospital.
Methods: A retrospective survey was conducted during February 2012- May 2012 at Ciptomangunkusumo hospital. Data was collected by using questionnaire. Subjects with ketoacidosis complication were included. Subjects without ketoasidosis were excluded.
Results: Of 193 children with diabetes mellitus in Indonesia, 71 subjects met the criteria. Most children were female (56.3%). Most subjects were 10–14 years old (46.4%) and 5–10 years old (22.5%). From all subjects, 39.4% had family history of type II DM and 9.8% had family history of type I DM. Most subjects were not obese (91.5%) with body weight are 26.04 ± 12.4 kg and body height are 130.7 ± 26.8 cm. Most subjects had one episode of DKA (60.5%), but 22.5% and 8.4% had two or three episodes. Hemoglobin A1c (HbA1c) is 12.3 ± 2.4% from all subjects. Most subjects survived and 4.2% died from DKA.
Conclusions: Most subjects were female, aged 10–14 years old. Small proportion of subjects had family history of DM. Most subjects had 1 episode of DKA. Most subjects were not obese with HbA1c 12.3 ± 2.4%. Mortality from DKA was 4.2%.
Keywords: Characteristics, diabetes mellitus, ketoacidosis.

P-243-122

Analysis of causative factors on the formation of lipohypertrophy in type 1 diabetes mellitus and their relation to HbA1c levels

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Objectives: To determine the effects of insulin injections and other factors on the formation of lipohypertrophy. To investigate the ability and knowledge of the patients on insulin injections and their preference of the injection site. To investigate the effect of lipohypertrophy on HbA1c levels.
Methods: Fifty-one patients (26 females, 25 males) with type 1 DM (T1DM) and lipohypertrophy aged between 3–18 (12.54 ± 3.1) years were included in the study. Mean age of diagnosis was 5.6 ± 2.7 years. All patients and their parents were asked to fill a questionnaire prepared by a pediatric diabetes nurse. Data were collected by reviewing medical records and outcomes of the questionnaire. Initial HbA1c levels were measured and then repeated 6 months later.
Results: The most preferred injection site by the patients was the upper arm. Only 25.5% of the patients were rotating injection sites regularly. Lipohypertrophy was mostly located in arms (72.5%). The most used pen needles were 31 Gx6 mm (45%). 43% of our patients were using a single pen needle more than two times. Insulin injections were applied by the patient in 43% of patients. In our study, 70.6% had a general knowledge on lipohypertrophy. Insulin was injected by wrong temperature in 45% of subjects, an unnecessary cleaning of injection site with disinfectants were in 59%. After 6 months, HbA1c levels remained unchanged (P = 0.311) in patients whose lipohypertrophies persisted, while there was a statistically significant difference in HbA1c levels (P = 0.026) in patients whose lipohypertrophies improved.
Conclusion: Insufficient and improper information and ability regarding insulin applications cause the formation of lipohypertrophy in T1DM. Lipohypertrophy and misapplication of insulin adversely affects the metabolic control in these patients. Diabetes education team should regularly review and control the knowledge of patients about insulin application techniques.

P-257-123

Carbohydrate metabolism in children with ß-thalassemia

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Objectives: The purpose of this study was to examine the frequency of carbohydrate metabolism in children with patients of homozygous ß-thalassemia, or disease Cooley. In the former USSR thalassemia is most common in Azerbaijan Republic (up to 7–10% of the population of individual low-lying areas of the country), some less - in Georgia, North Caucasus (especially Dagestan) in the Central Asian republics. In general, the distribution of the gene of thalassemia is due mainly to places where previously malaria-endemic and where widespread closely related marriages. Another important pathological process of determining the course of the disease, is the excessive accumulation of iron. A significant amount of iron ingested transfusions used to treat thalassemia, containing red blood cells. Develop iron overload of the body - the so-called ''Hemosiderosis'' all organs. The worst of the suffering heart, liver, skin and endocrine glands, in particular, the endocrine part of pancreas, which can lead to diabetes.
Methods: A survey was conducted 36 children with ß - thalassemia. For this purpose, identified the glucose tolerance test and fasting glucose. Of the surveyed 67% were boys, 33% girls. The average age of patients was 6.8 ± 0.62 years. Disease duration varied from year to 4-years and an average of 1.7 ± 0.25 years. Blood glucose was determined by blood glucose monitoring system MultiSure (Apex Biotechnology Corp.).
Results: Normal values of the glucose tolerance test was in 67% of children while 27% of the children was identified impaired glucose tolerance and 8% violation of glucose by the type of

diabetes. Current study was showed no correlation with the duration of the disease with age (r = 0.19), with blood glucose (r = -0.22).
Conclusion: According to our data we can say that carbohydrate metabolism is common for children with ß -thalassemia.

P-358-124

Helicobacter pylori infection in type 1 diabetes children and adolescents using 13C urea breath test

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Objectives: The prevalence of Helicobacter pylori (HP) infection in the general pediatric population in Poland is estimated by epidemiological studies at 10–15%. We designed the study to estimate the frequency of HP infection in children with type 1 diabetes (T1DM).
Methods: All patients of a regional out-patient diabetes clinic were invited to take part in this study. Finally there were 129 participants (72 girls) with T1DM. Following clinical data was ascertained: age, age at T1DM onset, HbA1c at study time, presence of gastroenterological symptoms (abdominal pain, halitosis, loss of appetite, nausea). HP infection was assessed by means of the Urea Breath Test (UBT) (IRIS, Wagner GMBH, Germany) after ingestion of 75 mg of 13C labeled urea. The results of the test were considered positive if 13C concentration [o/oo] raised in the exhaled air by more than 4.0.
Results: Mean age of the patients was 13.3 ± 3.5 years, disease duration - 4.43 ± 3.43 years and mean HbA1c of the patients - 7.45 ± 1.33%. Positive UBT results were obtained in 13 cases (10%). No differences between sexes according: age, T1DM duration, HbA1c and frequency of positive test results were found. Statistical analysis revealed also no influence of T1DM duration nor HbA1c on the UBT results. Additionally no significant relation to the reported symptoms could be determined.
Conclusions: Estimated prevalence of HP infection in T1DM children in Upper Silesia, Poland is not high and is comparable to healthy peers. HP infection does not seem to be related to the course of diabetes.
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P-22-125

Population awareness using posters prevents diabetic ketoacidosis in children at their initial presentation with type 1 diabetes

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Objective: We studied the effect of population education on the rate of diabetic ketoacidosis (DKA) in children (0–18 years) with newly diagnosed type 1 diabetes.
Research design and method: The rate of DKA at presentation was assessed for 2 years at Gosford (intervention site) and control centres. Then child care centers, schools and doctor's offices in Gosford were given posters and post cards on symptoms of type 1 diabetes in children. The rate of DKA at presentation was then assessed for 2 years.
Results: Two years before the education, 163 children were diagnosed with type 1 diabetes and the rate of DKA was 37.5% at all centres. During the 2 year education intervention, 29 children at Gosford were diagnosed with type 1 diabetes and 13.8% presented with DKA (c^2 = 4.74, P < 0.03). At the control centres 127 children were diagnosed and 38.6% presented with DKA.
Conclusion: Posters displayed in child care centres, schools and doctor's offices reduced the rate of DKA at initial diagnosis of type 1 diabetes in children by 64%.

P-179-126

Evaluation of serum magnesium & phosphorus in type 1 diabetic patients with diabetic ketoacidosis

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Introduction: During management of diabetic ketoacidosis, the there is no definite role for magnesium (mg), and phosphorus9ph), in most international guidelines.
Subjects and methods: 100 type 1 diabetic children with ketoacidosis (DKA), were studied for serum mg and ph, befre the starting of the manegemts and every 2 hours till complete cure from the DKA.
Results: The levels of ph in mg/dl at the start, then after 2 hours then at resolution of DKA, were: ph1 & ph2 & ph3 = 4.31 + 1.68, 2.9 + 0.99, 2.85 + 1.62 respectively. The levels of mg in mg/dl at the start, then after 2 hours then at resolution of DKA, were: mg1, mg2, mg3 = 2.49 + 0.53, 2.18 + 0.40, 2.12 + 0.46 respectively. There were highly positive relations between ph1 & Ph3, while there were no significant relations between ph2 and ph3. There were also highly significant positive correlations between mg1 and mg3, while there were no significant relations between ph2 and ph3.
Conclusions: It could be concluded from these results that there were significant decrease in the levels of serum mg and ph during the management of DKA and it could be recommended to start to focus on corrections of them in the international protocols of DKA management.

P-235-127

Type 1 diabetes with Down's syndrome are at high risk of coexistent autoimmunity

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The prevalence of comorbilities such as type 1 diabetes mellitus (T1DM), celiac disease (CD) and hypothyroidism is higher in Down's syndrome compared with the general population. The aim of our study is to describe the case of five diabetic patients with Down syndrome of whom 4 had one or more associated autoimmune diseases.
Results: We report five patients with Down syndrome among 2720 T1DM followed from 1975 to December 2011. Of these, 4 patients (80%) had T1DM and celiac disease association (T1DM-CD), (2 boys, 2 girls). Two of the 4 T1DM-CD had autoimmune thyroiditis. In Down'syndrome-T1DM-CD patients; the mean age at diabetes diagnosis was 9.8 ± 2.9 years (6.3; 12.5 years). The mean age at diagnosis of CD was 15.1 ± 6.8 years (9.6; 25 years). In one patient, CD and diabetes were diagnosed

simultaneously, in the 3 others, CD was diagnosed after a mean period of 6.9 ± 5.1 years (3.3; 12.8 years) after diabetes. CD occured in its classical presentation in the 4 patients (digestive disorders, short stature). The mean height at diagnosis of CD was -3.3 ± 1.2 SD (-4.4; -1.6 SD). One patient had hyperthyroidism, with positive anti-thyroperoxidase autoantibodies, and subsequently evolved to hypothyroidism, and the second had hypothyroidism revealed by goiter.

Conclusion: Celiac disease and autoimmune thyroiditis must be screened in patients with Down' syndrome in particular those with type 1 diabetes.

P-287-128

Dasman campaign for diabetic ketoacidosis prevention in children in Kuwait

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Objectives: Despite considerable advances in diabetes diagnosis, diabetic ketoacidosis (DKA) remains a serious complication associated with significant morbidity and mortality. The incidence of DKA in Kuwait is still high compared to the rest of the world. Between 1992 and 1994, a study showed that nearly half of the children (49%) with diabetes presented with DKA and in 23.5% it was severe (1). A decade later, 37.7% of children with newly- onset diabetes still presented with DKA and in 26% it was severe with a mortality of 0.15% (2). In 1999, a school and physician awareness campaign in Parma (3) has been shown to be effective in decreasing the frequency of DKA at presentation through shortening the latency period. This campaign centered on the earliest symptom of diabetes (nocturnal enuresis in a ''dry'' child) as reported by 89% of parents (4).

Methods: In order to shorten the period of carbohydrate intolerance preceding the diagnosis of type 1 diabetes, a similar campaign (displaying a poster of a child wetting his bed with a few practical messages) was initiated in Kuwait by displaying the Poster in Malls, Hospitals and Primary Health Care Centres where Family Physicians were given cards listing the early symptoms of diabetes to be given to parents. Displaying the Poster, mobile text messages and holding educational courses for school teachers were planned for kindergarten, primary and intermediary schools to alert parents and teachers on the early symptoms of diabetes in children.

Results: Success of the campaign will be measured by determining the incidence of DKA before and after the campaign through development of the Childhood Onset Diabetes eRegistry since January 1st 2011.

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P-301-129

Modern diagnostics of the complications appeared in the bone system in children with diabetes mellitus type 1

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Objectives: The research aims at finding out changes in mineral density of bones depending on the term of the type 1 diabetes mellitus in children with this disease and the status of recovery of it.

Methods: For this purpose, 25 patients with type 1 diabetes mellitus were taken to control. All patients were involved to the two measured X-Ray densitometric (QDR-4500A device manufactured by Hologic Company, USA) examination. The children were collected in 3 groups for the term of disease: 1thodst group - primarily found patients; 2nd group - ill children up to 5 years and 3rd group - children who are ill more than 5 years.

Results: No osteopenny/osteoporosis was found according to the (n = 5) densitometric indicators in the 1st group patients. Osteopenny (Z-score = -1 to -2.5) was found in 58.3% (n = 7) children in sub-recovery (HbA1c = 6.5–7.0%), osteoporosis (Zscore <-2.5) in 41.6% (n = 5) patients in derecovery (HbA1c >7.0%) state in the 2nd group. Osteopenny (Z-score = -1 to -2.5) was found in 37.5% (n = 8) children in sub-recovery (HbA1c ≥7.0%), osteoporosis (Zscore <-2.5) in 62.5% (n = 5) patients in derecovery state in the 3rd group.

Conclusion: According to our obtained indicators, Conducting of X-ray densitometry is considered as an additional diagnostic criteria depending on the term and recovery degree of the disease in children with type 1 diabetes mellitus and it allows finding out complications of the disease.

P-529-130

Diabetic ketoacidosis with acute renal failure and rhabdomyolsis: a case presentation and review of literate

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Objective: To present two cases of diabetic ketoacidosis, renal failure and rhabdomyolsis and provide a review of literature.

Methods: The 1st case a 7 years male patient presented with high grade fever disturbed conscious level. Patient was diagnosed as DKA as a first presentation for diabetes; by examination patient had metabolic acidosis high serum creatinine which not corrected by fluid replacement therapy and insulin infusion therapy on rate of 0.1 IU/kg/hour. Patient showed hyponatremia, hypophosphatemia, and hypokalemia. The 2nd case; a known diabetic female patient aged 15 years. She was diabetic since 3 years; she was maintained on basal-bolus regimen admitted by DKA precipitated by poor diet control and poor compliance on treatment. Also, she had disturbed sensorium, metabolic acidosis high serum creatinine which not corrected by fluid replacement therapy and insulin infusion therapy on rate of 0.1 IU/kg/hour. Patient showed hyponatremia, hypophosphatemia, and hypokalemia.

Results: After introduction of non-dialysis renal replacement patient starts to be controlled and serum creatinine starts to be corrected and both patients did not required renal dialysis.

Conclusion: Early introduction of non-dialysis renal replacement therapy in a case of sever acute renal failure in patients with DKA helps to improve clinical outcome.