

sodium 125 mmol/L (133–145), potassium 5.7 mmol/L (3.5–5.1), HCO<sub>3</sub> 20 mmol/L (21–31), anion gap 13 mmol/L (9–18), random glucose 141 mg/dL (70–199). Due to hyponatremia and dehydration, he was sent to a local emergency room where he was found to be mildly hypotensive at 87/57 mmHg. He received intravenous fluids for hydration and was sent home. On out-patient follow up, he appeared well despite being hypotensive. His additional labs revealed a random glucose of 330 mg/dl and elevated HbA<sub>1c</sub> of 8.3% (4.4–5.6). His urine was positive for glucose but negative for ketones. He was admitted for further management of new onset diabetes. On admission, he was well appearing and in no acute distress. Blood pressure was 86/57 mmHg, heart rate was 109 bpm, and other physical exam findings were unremarkable. Although his hyperglycemia improved after initiation of insulin therapy, his electrolyte abnormalities persisted, raising suspicion for adrenal insufficiency. An ACTH stimulation test was performed, with both baseline and 60-minute cortisol levels low at 1 ug/dl and 0.9 ug/dl, respectively, confirming adrenal insufficiency. He responded well to glucocorticoid and mineralocorticoid replacement. His electrolytes and blood pressure normalized. Further testing confirmed elevated levels of Glutamic Acid Decarboxylase antibodies 0.19 nmol/L (less than 0.02), Islet Antigen 2 Antibodies: 3.38 nmol/L (less than 0.02), and 21-Hydroxylase antibodies, consistent with T1D with concomitant Addison's disease (AD).

**Conclusion:** About 0.5% of patients with T1D have AD, but the diagnosis of T1D typically precedes AD for several years, thus the coexistence of both autoimmune conditions at diagnosis is rare.

## Diabetes Mellitus and Glucose Metabolism

### TYPE 1 DIABETES

#### *Association Between Serum Magnesium and Glycemic Control, Lipid Profile and Diabetic Retinopathy in Type 1 Diabetes*

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**Background:** Many studies have shown an association between decreased serum magnesium (Mg) levels and poor glycemic control and dyslipidemia in patients with type 1 diabetes (T1DM). However, few studies have evaluated the association between reduced Mg levels and the diabetes complications in these patients and, in particular with diabetic retinopathy (DR), found divergent results. **Aims:** To evaluate the status of serum Mg levels in adults with T1DM and to assess the association between Mg levels and glycemic control, lipid profile and prevalence of DR. **Methods:** Retrospective study of adults with T1DM, with an ophthalmological evaluation and a serum Mg level determination. According to Mg levels, the patients were stratified into two groups: normomagnesemic (1.81–2.60 mg/dl) and hypomagnesemic ( $\leq 1.80$  mg/dl) patients. Exclusion criteria were: patients on diuretics or proton-pump inhibitors,

malabsorption or diarrhea, oral magnesium supplementation in recent past, pregnancy or sepsis. **Results:** Included 105 patients (56.2% male) with median age of 36.0 (interquartile range 16.0) years and median T1DM duration of 16.0 (12.0) years. Median HbA<sub>1c</sub> was 7.6 (1.5)% and median Mg levels was 1.96 (0.23) mg/dl. Hypomagnesemia ( $\leq 1.80$  mg/dl) was detected in 20.0% (n=21) patients and 26.7% (n=28) had DR. Hypomagnesemic patients had higher HbA<sub>1c</sub> [8.2 (1.6) vs 7.5 (1.3)%, p=0.014]. There was no statistical difference in age, sex, T1DM duration or DR between the groups stratified by Mg levels. Mg levels was negatively and weakly correlated with systolic blood pressure (r=-0.200, p=0.041), HbA<sub>1c</sub> (r=-0.281, p=0.004) and BMI (r=-0.197, p=0.041). There was no correlation between Mg levels and total cholesterol, LDL-C, HDL-C or triglycerides. In multivariate logistic regression analysis, HbA<sub>1c</sub> was the only predictor of hypomagnesemia [OR=1.541 (1.027–2.312), p=0.037], after the adjustments for age, T1DM duration and BMI. There was no significant difference between patients with or without DR in relation to Mg levels [1.96 (0.28) vs 1.96 (0.19) mg/dL, p=0.986]. Also, there was no statistically significant association between Mg levels and the severity of DR or T1DM duration. In multivariate analysis, T1DM duration, male and estimated glomerular filtration rate  $>60$  mL/min/1.73m<sup>2</sup> had independently significant association with DR after adjusting for age, glycemic control, hypertension, dyslipidemia, 25-hydroxyvitamin D and Mg levels [OR=1.194 (1.088–1.310), p<0.001; OR=6.980 (1.654–29.450), p=0.008, and OR=0.780 (0.008–0.751), p=0.028, respectively]. **Discussion:** Hypomagnesemia is a common problem in adults with T1DM and it was correlated with glycemic control, although we did not find significant association between Mg levels and lipid profile or prevalence of DR. Future longitudinal studies may elucidate the causality between reduced Mg levels and the prevalence of diabetes complications.

## Diabetes Mellitus and Glucose Metabolism

### TYPE 1 DIABETES

#### *Chronic Kidney Disease Prevalence and Glomerular Filtration Rate Trends in Children With Type 1 Diabetes*

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**Background and Objectives:** Children with type 1 diabetes (T1D) are at risk for acute kidney injury (AKI) secondary to diabetic ketoacidosis, as well as chronic kidney disease (CKD) from diabetic nephropathy. The primary objective of this study was to assess the prevalence of abnormalities in estimated glomerular filtration rate (eGFR) in children with T1D. As a secondary objective, we sought to explore the relationship between clinical characteristics and trends in eGFR. **Design, Setting, Participants, and Measurements:** This ambispective cohort study involved children aged 18 years or younger with T1D (n = 420), followed in the diabetes clinic at British Columbia Children's Hospital (BCCH), the tertiary

pediatric hospital in Vancouver, British Columbia, Canada. Data was collected from the BCCH paper and electronic health records. CKD was defined as eGFR less than 60 mL/min/1.73 m<sup>2</sup>. Being at risk of CKD was defined as having a mildly decreased eGFR (60-90 mL/min/1.73 m<sup>2</sup>) and/or hyperfiltration (eGFR ≥140 mL/min/1.73 m<sup>2</sup>). eGFR was calculated using the modified Schwartz formula (36.5 x height in cm / serum creatinine in μmol/L). Linear regression analysis was used to describe the relationship between eGFR and duration of T1D. Covariates included in the analysis included sex, history of DKA, A1c, and BMI. **Results:** Of the 420 participants, 225 (54%) were male, with a median age at T1D diagnosis of 6.1 years and T1D duration of 4.8 years (range <1.0–15.0 years). One-hundred and eighty-six (44%) children were hospitalized for DKA, of which 89 (48%) developed AKI. No participants had an eGFR < 60 ml/min/1.73m<sup>2</sup>, and 317 (76%) had normal renal function. Fifty-one participants (12%) had an eGFR < 90 ml/min/1.73 m<sup>2</sup>, and 52 (12%) demonstrated hyperfiltration. When analyzed as a cohort cross-sectionally based on duration of T1D, there was a significant linear decline in eGFR of 1.4 ml/min/1.73 m<sup>2</sup> per year (95% CI -1.95, -0.87 ml/min/1.73 m<sup>2</sup>). **Conclusion:** In a large group of pediatric patients with type 1 diabetes, 24% were at risk for chronic kidney disease based on a mildly decreased GFR and/or hyperfiltration. The pattern of eGFR decline over time is concerning and relevant, as this cohort is at risk for CKD secondary to diabetic kidney disease. Strategies are needed to improve the follow-up and management of early CKD in children with type 1 diabetes to maintain their renal function into adulthood, and more studies are needed to quantify further change in eGFR in the young adult population.

## Diabetes Mellitus and Glucose Metabolism

### TYPE 1 DIABETES

#### *Dipeptidyl Peptidase-4 (DPP-4) Inhibitor Therapy in the Management of Latent Autoimmune Diabetes in Adults (LADA): A Systematic Review and Meta Analysis*

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**Objective:** Latent autoimmune diabetes in adults (LADA) has been shown in recent studies to have heterogeneous pathophysiology and phenotype. Although insulin is considered as the therapeutic choice for these patients, other antidiabetic drugs have been studied in terms of glycemic control and beta cell function preservation. In particular, dipeptidyl peptidase-4 (DPP-4) inhibitors have shown immunomodulatory effects in animal models since it was demonstrated a higher DPP-4 activity in patients with LADA compared to patients with Type 1 and Type 2 diabetes suggesting a possible effect on autoimmunity found in LADA. This study aims to review the outcomes of the included studies and evaluate the efficacy of DPP-4 inhibitors in the treatment of LADA. **Methods:** We searched Medline,

Embase, PubMed and Cochrane Library Databases and ClinicalTrials.gov for studies concerning the use of DPP4 inhibitors in patients with latent autoimmune diabetes in adults (LADA). **Results:** Preclinical studies demonstrated drug's immunomodulatory effects in terms of suppression of inflammatory processes and oxidative stress providing endothelial protection leading to improved metabolic control and prevention of vasculopathy. From this meta-analysis, pooled data from 8 randomized controlled trials revealed that the use of DPP-4 inhibitors in LADA patients resulted in an improved glycemic control, decreased insulin requirement and increased beta cell function as assessed by a decrease in GADA titers, increased C peptide levels and HOMA B. **Conclusion:** Beneficial effects of DPP4 inhibitors are shown by the included studies indicating that they are promising therapeutic agents for patients with LADA. However, caution should still be exercised since there is still much to learn about the disease itself and larger scale prospective randomized trials are needed to assess the efficacy and safety of DPP4 inhibitors for these patients.

## Diabetes Mellitus and Glucose Metabolism

### TYPE 1 DIABETES

#### *Effects of Treatment With Continuous Subcutaneous Insulin Infusion on Arterial Stiffness and Endothelial Glycocalyx Compared to MDI Intensification in Patients With Type 1 Diabetes: Improvement After a Six-Month Pump Treatment.*

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Patients with type 1 diabetes mellitus (T1DM) present signs of atherosclerosis and endothelial dysfunction earlier compared to healthy individuals. The evidence regarding the efficacy of continuous subcutaneous insulin infusion (CSII) in vascular function in T1DM are scarce. The aim of this study is to determine whether insulin intensification with CSII improves arterial stiffness and endothelial function in T1DM compared to multiple daily insulin (MDI) injections. Thirty patients with T1DM were included in our study. Fifteen patients with poor glycemic control were transitioned from MDI to CSII and were reviewed immediately prior (baseline) and six months after the initiation of CSII. Fifteen patients, matched for sex, age and glycemic control, remained on intensified treatment with MDI