

Vitamin D Status in Indigenous Youth with Type 2 Diabetes

MELISSA GABBS*^{1,2} ALLISON DART^{1,2}, FARRAH JABAR¹, KRISTINE KROEKER³, TOM BLYDT-HANSEN⁴, JON MCGAVOCK^{1,2}, BRANDY WICKLOW^{1,2} on behalf of the ICARE INVESTIGATOR TEAM

¹The Children's Hospital Research Institute of Manitoba ²Department of Pediatrics and Child Health, Faculty of Medicine, University of Manitoba ³Biostatistical Consulting Unit, George and Fay Yee Centre for Healthcare Innovation ⁴University of British Columbia

Objective: Low vitamin D (25[OH]D) status is associated with an increased risk for several conditions including type 2 diabetes (T2D). The association between 25[OH]D sufficiency and T2D in youth is unknown.

Research Design and Methods: A cross-sectional comparison of 25[OH]D status was performed among Indigenous youth with T2D (n=172) and overweight controls (n=53) within The Improving renal Complications in Adolescents with T2D through REsearch (iCARE) cohort. 25[OH]D status was classified as sufficient (≥ 50 nmol/L) or insufficient (< 50 nmol/L). Univariate and multivariate logistic regressions were performed.

Results: The cohort had a mean age of 15.4 ± 2.6 at baseline, 65.3% were female, and 72.9% were from rural communities. The majority of youth (79.1%) presented with insufficient 25[OH]D. Age, sex, glycemic control, obesity, and rurality were not associated with 25[OH]D status. In multivariate models, youth with T2D were 55% less likely to be sufficient in 25[OH]D (OR 0.45 [95% CI: 0.21, 0.96]). Data collected in the summer months (OR 3.04 [95% CI: 1.33, 6.96]) and self-reported 25[OH]D supplementation (OR 6.52 [95% CI: 2.30, 18.47]), were strong predictors of 25[OH]D status.

Conclusions: Youth with T2D and overweight controls have high rates of 25[OH]D insufficiency. Youth with T2D are less likely to be 25[OH]D sufficient compared to youth without T2D. Seasonality and 25[OH]D supplements strongly increase the odds of 25[OH]D sufficiency.

Determinants of readiness for adopting healthy lifestyle behaviours among Indigenous adolescents with type 2 diabetes: A cross sectional study

Jonathan McGavock¹⁻³, Anita Durksen², Brandy Wicklow¹⁻³, Sayma Malik⁴, Elizabeth AC Sellers¹⁻³, Tom Blydt-Hansen⁶, Dan Chateau⁵, Allison Dart¹⁻³

¹Department of Pediatrics and Child Health, Rady Faculty of Health Sciences, ²Children's Hospital Research Institute of Manitoba, ³Diabetes Research Envisioned and Accomplished in Manitoba Research Theme, ⁴Department of Clinical Psychology, ⁵Manitoba Centre for Health Policy Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba; Section of Nephrology, Department of Pediatrics BC Children's Hospital, Vancouver BC.

Introduction: The aim of this study was to determine if readiness for adopting healthy lifestyle behaviours was associated with mental health and co-morbid conditions in youth with type 2 diabetes (T2D). We hypothesized that adolescents who were ready to make positive changes in areas of physical activity and diet would have better mental health and lower levels of stress and distress.

Methods: A cross sectional comparison of various measures of mental health (distress, stress, resilience) and comorbid conditions (glycated hemoglobin, adiposity, hypertension) was conducted within a cohort of youth with T2D stratified according to their readiness to adopt healthy lifestyle behaviours.

Results: Within the entire cohort (n=141) only 14% were considered ready to adopt all healthy lifestyle behaviours. Readiness to adopt all lifestyle behaviours was associated with higher positive mental health (47 vs 39 units; $p < 0.05$) and sense of mastery (40 vs 37 units, $p < 0.05$), lower perceived stress (27 vs 29 units, $p < 0.05$) and distress (8 vs 10 units, $p < 0.05$) as well as better glycemic control (HbA1c: 8.4 ± 2.6 vs $9.7 \pm 2.8\%$; $p < 0.05$) compared to youth not ready to adopt all lifestyle behaviours.

Conclusion: Readiness for adopting healthy lifestyle behaviours is low among adolescents with type 2 diabetes. Being ready to adopt healthy lifestyle behaviours was associated with better mental health and glycemic control. This has significant implications for the approach to care of adolescents with type 2 diabetes.

Diabetes in Pregnancy Exposure, Mitochondrial Markers, and Diastolic Function in Adolescents with Type 2 Diabetes

LAETITIA GUILLEMETTE*¹, ALLISON DART¹, BRANDY WICKLOW¹, VERNON W. DOLINSKY¹, DAVINDER JASSAL², ELIZABETH SELLERS¹, TODD A. DUHAMEL², JONATHAN MCGAVOCK¹

¹Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, Manitoba; ²Institute of Cardiovascular Sciences, St. Boniface Hospital Research Centre, Winnipeg, Manitoba.

Purpose: Mitochondrial dysfunction is intimately linked to type 2 diabetes (T2D) and cardiovascular disease (CVD). We hypothesized that exposure to diabetes in pregnancy (DiP) would adversely affect mitochondrial function and CVD risk in youth with T2D.

Methods: We analysed serum metabolomic markers of mitochondrial function/oxidative stress (ultra-performance liquid chromatography-tandem mass spectroscopy) as well as cardiac diastolic function (echocardiography-measured left ventricular early-to-late [E/A] blood flow velocity) in youth with T2D. DiP exposure was classified as T2D (n=34), gestational diabetes (n=16), and normoglycemia (NG; n=38). Significance was set at q (p-value adjusted for false discovery rate)<0.05.

Results: Groups were similar for sex (62 vs 43 vs 71% female), age (14.8±2.7 vs 15.4±2.8 vs 15.4±2.6 years), duration of diabetes (3.0, [interquartile range]: [2.0-5.0] vs 2.0 [1.0-3.5] vs 3.0 [2.0-5.0]years), fat% (30±10 vs 31±10 vs 33±13%) and systolic blood pressure load (45 [22-74] vs 42 [24-53] vs 33 [19-61]%). DiP exposure was not associated with metabolomic markers of mitochondrial function but worsened oxidative stress (hydroxyoctadecadienoic acids [13-/9-HODE]; T2D/NG ratio=2.20, q=0.02; methionine sulfoxide T2D/NG ratio=2.06, q=0.01). Mitochondrial metabolomic markers were not associated with diastolic function (leucine: r= -0.23, q=0.08; isoleucine: r= -0.25, q=0.06; valine: r= -0.22, q=0.09; carnitine: r=0.19, q=0.13). Oxidative stress was inversely associated with diastolic function (13-/9-HODE: r= -0.23, q=0.08; methionine sulfoxide: r= -0.23, q=0.08).

Conclusion: Oxidative stress, but not mitochondrial dysfunction, is associated with DiP exposure and impaired diastolic function in adolescents with T2D.

Progression and Regression of Albuminuria in Youth with Type 2 Diabetes

FARRAH JABAR^{*1}, BRANDY WICKLOW^{1,2}, JONATHAN MCGAVOCK^{1,2}, ELIZABETH SELLERS^{1,2}, TOM BLYDT-HANSEN³, KRISTINE KROEKER⁴, DAN CHATEAU⁵, ALLISON DART^{1,2} for the iCARE Investigator Team

¹The Children's Hospital Research Institute of Manitoba ²Department of Pediatrics and Child Health, Faculty of Medicine, University of Manitoba ³University of British Columbia ⁴Biostatistical Consulting Unit, George and Fay Yee Centre for Healthcare Innovation ⁵Manitoba Centre for Health Policy

Background: Youth with type 2 diabetes (T2D) are at high risk for progression to end-stage kidney disease. The natural history of proteinuria over time is unknown.

Objectives: Evaluate changes in albuminuria status over time and associated risk factors.

Methods: Baseline clinical factors and plasma and urine cytokines were compared among 124 youth with T2D from The Improving renal Complications in Adolescents with T2D through REsearch study stratified by changes in albuminuria at last follow-up: normal [albumin:creatinine ratio (ACR) <2mg/mmol]; progression [normal to \geq 2mg/mmol OR 2-<20 to \geq 20mg/mmol]; regression (\geq 2 to <2 OR \geq 20 to 2-<20mg/mmol); and persistent (remained in same ACR category).

Results: Median ACR was 0.72 mg/mmol at baseline, 1.2 at 1 year (n=31), 1.7 at 2 years (n=70), 2.3 at 3 years (n=20). At last follow-up, 48.4% remained normal, 26.6% progressed, 8.1% reverted, and 16.9% had persistent albuminuria. Compared to normal, progression and persistent albuminuria were associated with longer duration of diabetes (1.7 vs. 1.8 vs. 3.4 years, respectively; p=0.02), higher HbA1c (8.8 vs. 9.2 vs. 10.8%; p=0.0006), and higher systolic (20.6 vs. 28 vs. 57%; p=0.003) and diastolic (9.3 vs. 15.8 vs. 19.6% p=0.006) blood pressure loads (% of time >95th %ile). Cytokines did not predict albuminuria status (n=50). Reverters were more likely to be on an ACE inhibitor (p<0.00001).

Conclusions: Youth with T2D have high rates of albuminuria. Traditional risk factors predict worsening albuminuria. Larger sample sizes are needed to evaluate cytokine profiles.

Diabetes in Pregnancy Exposure, Mitochondrial Markers, and Diastolic Function in Adolescents with Type 2 Diabetes

LAETITIA GUILLEMETTE*¹, ALLISON DART¹, BRANDY WICKLOW¹, VERNON W. DOLINSKY¹, DAVINDER JASSAL², ELIZABETH SELLERS¹, TODD A. DUHAMEL², JONATHAN MCGAVOCK¹

¹Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, Manitoba; ²Institute of Cardiovascular Sciences, St. Boniface Hospital Research Centre, Winnipeg, Manitoba.

Purpose: Mitochondrial dysfunction is intimately linked to type 2 diabetes (T2D) and cardiovascular disease (CVD). We hypothesized that exposure to diabetes in pregnancy (DiP) would adversely affect mitochondrial function and CVD risk in youth with T2D.

Methods: We analysed serum metabolomic markers of mitochondrial function/oxidative stress (ultra-performance liquid chromatography-tandem mass spectroscopy) as well as cardiac diastolic function (echocardiography-measured left ventricular early-to-late [E/A] blood flow velocity) in youth with T2D. DiP exposure was classified as T2D (n=34), gestational diabetes (n=16), and normoglycemia (NG; n=38). Significance was set at q (p-value adjusted for false discovery rate)<0.05.

Results: Groups were similar for sex (62 vs 43 vs 71% female), age (14.8±2.7 vs 15.4±2.8 vs 15.4±2.6 years), duration of diabetes (3.0, [interquartile range]: [2.0-5.0] vs 2.0 [1.0-3.5] vs 3.0 [2.0-5.0]years), fat% (30±10 vs 31±10 vs 33±13%) and systolic blood pressure load (45 [22-74] vs 42 [24-53] vs 33 [19-61]%). DiP exposure was not associated with metabolomic markers of mitochondrial function but worsened oxidative stress (hydroxyoctadecadienoic acids [13-/9-HODE]; T2D/NG ratio=2.20, q=0.02; methionine sulfoxide T2D/NG ratio=2.06, q=0.01). Mitochondrial metabolomic markers were not associated with diastolic function (leucine: r= -0.23, q=0.08; isoleucine: r= -0.25, q=0.06; valine: r= -0.22, q=0.09; carnitine: r=0.19, q=0.13). Oxidative stress was inversely associated with diastolic function (13-/9-HODE: r= -0.23, q=0.08; methionine sulfoxide: r= -0.23, q=0.08).

Conclusion: Oxidative stress, but not mitochondrial dysfunction, is associated with DiP exposure and impaired diastolic function in adolescents with T2D.

IGFBP-2 is associated with type 2 diabetes and renal health measures in youth.

JONATHAN MCGAVOCK¹, MARC-ANDRE NOLAN², LAETITIA GUILLEMETTE¹, JANA SLAGHT^{1*}, BRANDY WICKLOW¹, FREDERIC PICARD², ALLISON DART¹ AND THE ICARE INVESTIGATOR TEAM

¹Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, Manitoba; ² Institut universitaire de cardiologie et de pneumologie de Québec - Centre de recherche de l'Université Laval, Québec, Qc.

Purpose: Insulin-like growth factor binding protein-2 (IGFBP-2) is a robust biomarker of type 2 diabetes (T2D) in adults. The purpose of this study was to determine if IGFBP-2 is associated with T2D and renal health markers in youth.

Methods: Multivariate linear regression was used to compare serum IGFBP-2 concentrations between youth with T2D with normoalbuminuria (n=23), peers with microalbuminuria (n=33) and normoglycemic youth matched for gender, sex, and ethnicity (n=10). Bivariate regression tested for associations between IGFBP-2 and 24-hour blood pressure, glycemic control, and urine and serum markers of inflammation.

Results: Youth with T2D (n=56) and controls (n=10) were matched for age (15.1±1.6 vs 15.1±1.9 years) and body mass index z-score (2.9±0.8 vs 2.5±1.0). After adjusting for confounding, IGFBP-2 levels were lower in youth with T2D compared to controls (106±6 vs 180±15 ng/mL, p<0.01). Among youth with T2D, IGFBP-2 was modestly lower among youth with microalbuminuria compared to youth with normoalbuminuria (98±6 vs 112±5 ng/mL, p=0.09). Serum IGFBP-2 was associated with HbA1c (r= -0.3, p=0.03), albumin to creatinine ratio (r=-0.34, p=0.01) and urinary CXCL10 (r=0.59, p=<0.001). IGFBP-2 was not associated with hypertension, dyslipidemia, measures of oxidative stress or inflammation (TNF1α, urinary IL-18 and IL-6, CRP).

Conclusion: In this pilot study, IGFBP-2 is associated with T2D and measures of renal health in youth with T2D. Results need to be confirmed in a larger sample.