ISPAD-Breakthrough T1D Fellowship 2024– Progress Report

Fellowship awarded to: Julia Mercer, RD CDE Diabetes Clinic, Alberta Children's Hospital, Calgary, AB Canada

Mentor: Daniele Pacaud, MD FRCPC Division of Endocrinology Department of Pediatrics, Cumming School of Medicine, University of Calgary, Alberta Children's Hospital, Calgary, AB Canada

Start of fellowship: April 1, 2025

Project: Does Use of Protein Supplements in Children with Type 1 Diabetes Impact Kidney Health?

Background: Diabetes is the leading cause of kidney disease in Canada. Nationally, there are 1 in 300 school age children with Type 1 Diabetes and the incidence is increasing. The Alberta Children's Hospital Diabetes Clinic has noticed a considerable number of children and teens using protein supplements (protein powder, protein bars, shakes and higher protein milks) to help improve nutrition, promote weight gain, increase muscle mass or improve athletic performance. Diabetes Canada Clinical Practice Guidelines (CPGs) state that macronutrient distribution is flexible within recommended ranges and will depend on individual treatment goals and preferences. For children, it is suggested that they follow eating patterns as outlined by Eating Well with Canada's Food Guide. However, we know that children with diabetes tend to eat similarly to those without diabetes- and that nutritional intake is often suboptimal. Regarding protein intake, the CPGs suggest families choose lean animal proteins, and particularly more vegetable protein foods. No statement is given regarding the use of protein supplements. ISPAD (International Society for Pediatric and Adolescent Diabetes) Clinical Practice Consensus guidelines state there is minimal evidence on use of protein or other nutritional supplements to support athletic performance in adolescents and that protein supplementation should not be routinely recommended for youth. The American Diabetes Association (ADA) Standards of Care does not recommend taking supplements and does suggest taking into consideration if there might be harm in doing so. Given that increased protein intake can impact renal function, a literature review was completed using the key words of "protein supplement use and Type 1 Diabetes", "Type 1 diabetes and dietary protein intake" (in adults and adolescents), and "Type 1 diabetes supplement use in adolescents".

In clinical practice, measurement of renal function is done by analyzing urine and blood creatinine and, through use of accepted formulas, estimating the glomerular filtration rate (eGFR). Stimulated glomerular filtration rate, also called renal reserve, is obtained through serial measurement of eGFR before and after a protein load. Both adult and pediatric studies have shown that measuring stimulated eGFR is more sensitive to detect early renal impairment (Bosch et al, 1983 ; Bosch et al 1984; Cleper et al 1997). Further in recent years, emerging information suggest that using cystatin-c instead of creatinine is more accurate and less likely to be affected by non-renal causes than creatinine (Nwanyonenyi, NV et al, 2024; Pizzo et al 2024). However, there are some studies that suggest cystatin-c may not detect changes in eGFR with a protein load (Mueller, T. F., et al 2009 and Rodenbach et al 2017). Finally, there is no study comparing renal reserve calculated from creatinine measurements and cystatin-C measurements.

Many studies reviewed recognize that use of protein supplementation is increasing and acknowledge that although there are benefits, caution should be used particularly due to the potential impact on renal function. Several articles mention that people with Type 1 Diabetes are at risk of nephropathy and one suggests screening should be completed annually (Favel 2022). Further studies are needed to assess use of protein supplements in teens with Type 1 Diabetes and its potential impact on renal function. Confirming overall protein intake (from food and supplements) would also help to determine if teens are consuming more than the RDA. Information gathered will be useful for families to help guide their decisions about protein supplement use and for the clinic to help with consistent messaging. The purpose of this study is to assess protein supplement use and impact on renal function reserve (RFR).

Objective: to assess use and intake of protein supplements and determine the impact of increased protein load on kidney function/health.

Research Question: Does use of protein supplements impact kidney health in children with Type 1 Diabetes?

Hypothesis: In our clinic population, use of protein supplements in children with Type 1 diabetes will affect renal function reserve.

Specific aims of the pilot study:

1) To test the study procedure for feasibility
2) To obtain preliminary data on frequency of use and effect on renal reserve prior to planning a lager, possibly multicenter study on this topic

3) To compare use of creatinine and cystatin-C in measurement of renal reserve

Methodology:

*Study Population***:** children age 10-17.9 years of age with Type 1 Diabetes who are followed in the Alberta Children's Hospital Diabetes Clinic. The goal is to enroll 20 patients, those that are already consuming protein supplements and those that are not. This observational pilot study will consist of a convenience sample to examine the feasibility of the methodology for a larger study.

Study Design: cross-sectional observational study.

Study Protocol

At Baseline Visit:

1. **give consent to participate in the study**
2. **confirm eligibility criteria**
3. **provide demographic information (**age, gender, date of birth, date of diagnosis)**.**
4. **Obtain anthropometrics and vital signs** (height and weight, blood pressure, heart rate).

Renal Reserve Testing (as outlined by Cleper et al, Pediatr Nephrol (1997) 11: 473–476): in brief, this involves, after an overnight fast, collecting blood and urine samples at baseline and after giving an oral protein load (1 gr/kg of body weight, up to a max of 80g).

	-2 h	-1 h	0 h	+ 1 h	+ 2 h
Water Intake	X	X	X	X	X
Protein Intake			x		
Urine Collection	X	x	X	X	x
Blood Collection		X			x

Surveys and Questionnaires- to be completed during downtime

a) Sports Supplement Survey: All participants will complete a survey on sports supplements and a food frequency questionnaire to assess protein intake from food.

b) **Food Frequency Questionnaire to assess protein intake from the child's diet:** The standard Block Kids 2004 FFQ was developed in a scientific and data-based way and has been extensively studied and validated.

Statistical Methods:

Statistical Analysis

Descriptive statistics will be tabulated. Data will be presented as median with lower and upper quartiles for continuous variables or as number and percentages for binary or categorical variables. Fasting eGFR and renal reserve will be compared between those who use supplements and those who do not with a Student T test.

In exploration analysis, a regression analysis will be used to correlate renal reserve and total protein intake correcting for age, sex, and duration of diabetes.

Bland-Altman plot analysis will be used to assess the level of agreement between creatinine and cystatin-C eGFR values.

Sample Size Estimates:

As we do not know the frequency of use of protein supplement use and the impact it may have on renal function we cannot calculate a sample size yet. This pilot study will generate the data to be able to determine more accurately the sample size for a properly numbered study.

Current Status:

The first few months were dedicated to establishing the methodology and protocol, looking for nutrition surveys and a validated FFQ, and preparing submission for Ethics.

The study involves substantial budget costs, which are critical to the protocol. To reduce the burden on participants, a research nurse will be responsible for administering IVs and assisting with blood and urine sample collection. Laboratory analyses—including urine creatinine, serum creatinine, and urine albumin, along with associated administrative fees—will be conducted by Alberta Precision Laboratories. The Cystatin C measurement kit was procured separately, and a lab technician will be compensated to perform the ELISA assay.

Study Budget:

A. Research Procedure Costs				
Service/Procedures	**Quantity**	**Cost Per Item**	**Number of Participants**	**Total Costs**
Informed consent				
Questionnaires	20	$35	20	$700
Hematology/Chemistry/Urinalysis	Elisa (ALPCO)			$1,500
Labs- APL (urine creatinine, serum creatinine, urine albumin + admin fee)			20	$1,985
protein drink	2 cases	$0	20	$100
Vacutainers, urine collection cups	100			$75
			Sub-Total	4360
B. Personnel Costs				
Personnel	**cost per Visit**	**Total Visits**	**Number of Participants**	**Total Costs**
Research Assistant	$60/hr x 7h	7	20	$2,940
Physician (reimbursement for service)	0			0
Travel to present the pilot study (expected as part of award)				$3,000
Lab Tech (to run Elisa)	$35/hr x 7h	1		$245
			Sub-Total	6185
C. Non-Procedure Costs				
Service/Cost	**Quantity**	**Cost per Item**	**Number of Participants**	**Total Costs**
Participant reimbursement (e.g. parking)		$15	20	$300
Participant payment (e.g. $50/visit)		$25	20	$500
			Sub-total	800
			Total Study Cost	11345

Ethics approval was received on June 18, 2025. Administrative approval for research to proceed was granted September 11, 2025.

Next steps will be recruitment of participants for the study (there are currently 5 enrolled), data collection and analysis. The anticipated timeline is 6 months. The ambition is to submit an abstract for ISPAD 2026 with the results from this study.

References:

Annan, S; Higgins, L et al. 2022 ISPAD Clinical Practice Consensus Guidelines 2022: Nutritional Management in Children and Adolescents with Diabetes

Cleper, R, Davidovitz, M, Halevi, R, Eisenstein, B. Renal functional reserve after acute poststreptococcal glomerulonephritis. Pediatr Nephrol (1997) 11:473-476.

Delimaris, I. Adverse Effects Associated with Protein Intake above the Recommended Dietary Allowance for Adults. ISRN Nutr 2013; 2013: 126929. 2013 Jul 18. Doi: 10.5402/2013/126929

Dorsch, K. D., & Bell, A. (2005). Dietary supplement use in adolescents. Current Opinion in Pediatrics, 17(5), 653-657.

Favel K, Irvine M, Ronsley R, Panagiotopoulos C, Mammen C. Glomerular Filtration Rate Abnormalities in Children With Type 1 Diabetes Can J Diabetes. 2022 Jul;46(5):457-463.e1.

Gaebe K, White C, Mahmud F, Scholey J W, Elia Y, Sochett E, Cherney D. Evaluation of novel glomerular filtration rate estimation equations in adolescents and young adults with type 1 diabetes J Diabetes Complications. 2022 Jan;36(1):108081.

Jovanov, P., Đorđić, V., Obradović, B. *et al.* Prevalence, knowledge and attitudes towards using sports supplements among young athletes. *J Int Soc Sports Nutr* 16, 27 (2019)

Ibrahim RB, Srivaths P, Tam E, Devaraj S. Utility of Cystatin C-based Equation for the Estimation of Glomerular Filtration Rate in a Pediatric Population. J Appl Lab Med. 2024 Jul 1:9(4) 803-808 doi: 10.1093/jalm/jfae034 PMID: 38656545

Lejk A, Mysliwiec M, Mysliwiec A. Can athletes with type 1 diabetes use supplementation? Czy Sport z cukrzyca typu 1 moga stosowac odzywki? [Internet]. 2020;26(2):97–103

Lesgards, Jean-Francois. Benefits of Whey Proteins on Type 2 Diabetes Mellitus Parameters and Prevention of Cardiovascular Diseases. Nutrients 2023 Mar 6;15(5):1294. doi: 10.3390/nu15051294.

Mueller, T.F., Raeder, J., Oettl, K., Zitta, S., Klausmann, G., Estelberger, W., Reibnegger, G. Cystatin C Does Not Detect Acute Changes in Glomerular Filtration Rate in Early Diabetic Nephropathy. Renal Failure, 2008;30(10):21-29

Muntis FR, Smith-Ryan AE, Crandell J, Evenson KR, Maahs DM, Seid M, et al. A High Protein Diet Is Associated with Improved Glycemic Control Following Exercise among Adolescents with Type 1 Diabetes. Nutrients [Internet]. 2023;15(8)

Nwanonanyim NV, Ijoma CK, Arodiwe E, Nwanonenyi MI, Nebo C.
Diagnostic Performance of Cystatin C in the Early Detection of Diabetic Kidney Disease at the University of Nigeria Teaching Hospital, Ituku-Ozallo. Cureus.2024 Oct23;16(10):e72230.doi:10.7759/cureus.72230 PMID 39502964; PMC 11537672

Patel V, Aggarwal K, Dhawan A, Singh B, Shah P, Sawhney A, et al. Protein supplementation: the double-edged sword. Proc (Bayl Univ Med Cent) [Internet]. 2024;37(1):118–26

Pizzo H, Nguyen J, Schwartz GJ, Weseling-Perry K, Ettenger R, Chambers ET, Weng P. Comparison of estimated GFR using cystatin C versus creatinine in pediatric kidney transplant recipients. Pediatr Nephrol. 2024 Jul; 39(7): 2177-2186. Doi 10.1007/s00467-024-06316-6. Epub 2024 Mar1. PMID: 38427073; PMCID: PMC11147893
Paterson MA, King BR, Smart CEM, Smith T, Rafferty J, Lopez PE. Impact of dietary protein on postprandial glycaemic control and insulin requirements in Type 1 diabetes: a systematic review. Diabet Med [Internet]. 2019;36(12):1585–99

Rodenbeck KE, Fuhrman DY, Maier, PS et al. Renal response to a protein load in healthy young adults as determined by iohexal infusion creatinine clearance cimetidine-inhibited creatinine clearance and Cystatin C estimated glomerular filtration rate. J Ron Nutr 2017:21:275-281.

Rubin D, Bosy-Westphal A, Kabisch S, Kronsbein P, Simon M-C, Tombek A, et al. Nutritional Recommendations for People with Type 1 Diabetes Mellitus. Exp Clin Endocrinol Diabetes [Internet]. 2023;131(1–02):33–50

Shane-McWhorter, L. (2009). Dietary supplements for diabetes: an evaluation of commonly used products. Diabetes Spectrum, 22(4), 206-213

Sievenpiper, J; Chan, C, Dworatzak, P; Freeze, C; Williams, S. Nutrition Therapy, Chapter 11, Diabetes Canada Clinical Practice Guidelines. 2018 p564-579.

Wherett, D; Ho, J; Huot, C; Legault, L; Nakhla, M; Rosolowsky, E. Type 1 Diabetes in Children and Adolescents Diabetes Canada Clinical Practice Guidelines Expert Committee 2018