2024 ISPAD- Breakthrough T1D Research Fellowship Mid-term Report

Project Title: TYPE 1 DIABETES CHRONIC COMPLICATION PREVALENCE AND RELATION TO CONTINUOUS GLUCOSE MONITORING GLYCEMIC MEASUREMENTS IN UGANDAN YOUTH

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1.Background

Chronic diabetes complications contribute to significant lifetime morbidity and mortality, including devastating outcomes such as kidney failure, blindness, amputations and death from coronary artery disease. Early diagnosis of microalbuminuria (MA) and diabetic retinopathy (DR) is important because effective treatments exist to limit the progression to renal failure and blindness. Control of elevated cholesterol levels may help prevent cardiovascular disease. Recognition of peripheral neuropathy may encourage institution of measures to help prevent diabetes foot disease and amputation. In the US and other high-income countries, T1D complications are expected to generally take at least 5 years to develop after diabetes onset, and thus it is recommended that annual screening begin at this time (1). Screening for diabetes complications is very limited in low-income countries due to financial constraints.

Glycemic control in Ugandan youth with type 1 diabetes (T1D) is poor with high haemoglobin A1c (HbA1c) levels and wide swings in hyper- and hypoglycemia (2). Limited available data suggest that chronic T1D complications appear earlier in African youth compared to those from high income countries (3, 4), but screening is rarely affordable and thus data are sparse. Elevated HbA1c, a presumed surrogate for average glucose levels (AG), is associated with complications but in our population the HbA1c-AG relation is unpredictable(2, 5), and continuous glucose monitoring (CGM) parameters more accurately reflect individual glycemic patterns and stability. However, CGM is currently unattainable for most East Africans. Poor diabetes control places these youth at risk for microvascular and macrovascular complications.

In a pilot CGM study of 78 Ugandans age 4-26 years, average HbA1c was 10.9±2.7% (96±30 mmol/mol). Blinded CGM demonstrated only 30±19% of time was spent in the target range (70-180 mg/dL; 3.9-10 mmol/L), and 7±8% of time was spent in level 2 hypoglycemia (glucose <54mg/dL, 3.0 mmol/L). The coefficient of glucose variation was particularly high at 48±21% (CV>36% is considered glycemic instability) (2). Recent data suggest an association between glucose variability, MA and retinopathy (6). However, accurate assessment of these parameters requires CGM, an expensive approach that is rarely available in low-income countries. These data will provide a better understanding of the burden of chronic T1D complications in our setting and its risk factors, to help inform guidelines for screening and intervention.

SIGNIFICANCE

This complications study offers the unique opportunity to leverage the research infrastructure from Diabetes in African Youth: Improving Glucose Time-In-Range (DAYTime) to perform a cross-sectional assessment of chronic diabetes complications in Ugandan youth with T1D and correlate these findings with extensive CGM data and not only HBA1c. Understanding the burden of diabetes complications and its risk factors will help us develop screening and intervention guidelines that are appropriate for our low/low-middle income setting. We anticipate being able to maintain longitudinal follow up of these youth and children in the future and refer those with complications for early

intervention. These data will provide a better understanding of the burden of chronic T1D complications in our setting and its risk factors, to help inform guidelines for screening and intervention.

2. Research Hypothesis, key aim and objectives.

Hypotheses:

- *Chronic T1D complications are more prevalent in Ugandan youth and occur earlier in the course of disease compared to what is reported for youth with T1D residing in high income countries.*
- *CGM measures (times-in-range and coefficient of variation-CV) will correlate with the presence of complications; the correlation with CGM measures, will identify those who will benefit from CGM use in our setting even though intermittently.*

Aim:

To determine the prevalence of T1D complications and its relation to metabolic control using CGM data in youth in Uganda.

Specific Objectives

1. To determine the prevalence of microalbuminuria, retinopathy, neuropathy, hypertension and hyperlipidemia among children and youth (age 4-26 yrs) with Type 1 diabetes at Mulago and Nsambya T1D clinics
2. To assess the relationship between chronic diabetes complications and HbA1c and CGM measures (glucose time in the standard CGM ranges, AG, CV) among children and youth (age 4-26 yrs) with Type 1 diabetes at Mulago and Nsambya T1D clinics.

3.Project Plan

DAYTime Study: This study will leverage the research infrastructure of Diabetes in African Youth: Improving Glucose Time-In-Range (DAYTime) study to perform a cross-sectional assessment of chronic diabetes complications in youth with extensive CGM metabolic data. DAYTime study, is a Randomised clinical Trial which uses CGM to test hypothesis that CGM monitoring of youth with T1D for 6-12 months will improve their glycemic control compared to self-monitoring of blood glucose (SMBG) with a meter 3X per day. The NIH # R01DK126726 funds the work. This clinical trial was started in 2022 and has to date enrolled ~ 130 of the 180 participants. The participants are ages 4- 26 yrs with T1D for at least a year and are attending largest T1D clinics in Kampala at Mulago and Nsambya hospitals.
We will enroll children and young adults with T1D who are participating in DAYTime and some additional participants who are not part of the DAYTime cohort in order to accrue the required sample size for this study.

A sample size of 280 participants was calculated therefore we need extra participants outside of the DAYTime study.

We will collect cross sectional data from the participants for retinopathy screening, urine albumin creatinine ratio, lipid profile, Peripheral neuropathy examination, blood pressure measurement and physical examination including anthropometry**. (Table 1)**

Statistical Analysis

Proportion of children with the outcome (retinopathy, microalbuminuria, neuropathy, abnormal lipids) of the total children enrolled will be calculated. Multivariate logistic regression analysis will be done to determine the factors associated with retinopathy, microalbuminuria, and other complications; factors like duration of diabetes, HBA1c, CV, TIR, age. Etc. Other endpoints will be correlations of complications with CV and TIR. Linear regression models will be used to test the association between TIR and mean glucose, and the different complications.

4.Current Status of Research Work (January 2025 – September 2025)

Despite leveraging data from an existing study, we needed to seek ethical approval for the additional study procedures and also for the additional participants who will be enrolled and are not part of DAYTime study.

Ethical approval for this study was obtained; Uganda: MHREC 2025 – 276 (on 25th June 2025), UNCST: HS5723ES (7th August 2025), University of Minnesota: STUDY00024998 (10th June 2025).

I have now completed following tasks:

- Started data collection in August 2025 and have enrolled 80 participants of the 280 (~29%) of the sample size.
- Data entry of the collected data is ongoing.
- Presentation of the study project has been done at the the department of pediatrics, Makerere University.

Challenges

- Delays in obtaining the ethical approvals from the local research ethics Committees despite submitting the proposals early
- Interruption in the funding for the DAYTime study; since it is funded by the NIH and some of our data and participants were to be enrolled from this trial.

Table 1: shows the study procedures

Overview of Study Procedures	Day 1	Day 7-14
Informed Consent/Assent	**X**	
Eligibility including medical history, physical exam, BP measurements	**X**	
Medical/ sociodemographic questionnaire	**X**	
POC HbA1c	**X**	
Spot urine collection - Microalbumen	**X**	
Lipid profile	**X**	
Neuropathy exam	**X**	
Neuropathy Questionnaires (MNSI &GCSI)	**X**	
Retinopathy screening		**X**
CGM device placement	**X**	**X**
CGM removal		**X**
CGM device upload		**X**
Review CGM data and results with patient		**X**

References

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