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Original Article

Current clinical status, glucose control, and complication rates of children and youth with type 1 diabetes in Rwanda

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Objective: To describe the clinical status of youth and adolescents (≤ 25 yr) in the Rwanda Life For A Child (LFAC) program who had their first HbA1c measure in 2009 or 2010, and to identify factors which may relate to glycemic control (HbA1c) and complication status.
Research Design and Methods: Data were collected from June 2009 to November 2010 for the LFAC program in Rwanda and comprise clinical data from when participants' first HbA1c reading was obtained.
Results: From June 2009 to November 2010, 286 youth aged ≤25 yr had their first HbA1c. Mean age, duration, and age at diagnosis were 18.6 ± 4.5 yr, 3.4 ± 3.1 yr and 15.1 ± 4.8 yr, respectively. Mean HbA1c was 11.2 ± 2.7% with 15.7% (n = 45) having HbA1c <8%, while 30.8% (n = 88) had HbA1c >14%. Five (2.1%) had either abnormal tuning fork vibratory sensation or monofilament response, 21% (n = 31) had microalbuminuria (MA, A/C ratio >30 mg/g) and 5% (n = 7) had nephropathy (A/C ratio >300 mg/g). Diabetes duration and insulin dose/kg were positively associated with higher HbA1c, while residing in the southern province was associated with lower HbA1c. Duration, diastolic blood pressure, and HbA1c were positively associated with developing MA, while age was protective.
Conclusions: These data from the LFAC program for 2009–2010 show that there is a urgent need for dramatically improved care, as many patients have greatly elevated HbA1c measures, often >14%. We have identified correlates of better control (e.g., living in the Southern province) and MA (e.g., diastolic blood pressure), which provide potential avenues to improved quality of care.

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Diabetes is a non-communicable disease of growing global concern. It is projected that 380 million people world-wide will be affected by this disease by 2025, with 18.7 million residing in sub-Saharan Africa (1). This disease is an especially large problem for people living in developing countries where access to diabetes care and necessary insulin are limited. These barriers lead to poor glycemic control, which may result in severe or fatal complications (2).

Rwanda is a country located in the Great Lakes Region of East Africa and has a population of approximately 11.3 million people within 26338 km^2, making it the most densely populated country in Africa (3). Though Rwanda has made great progress economically and socially since the 1994 genocide, 56.7% of Rwandans still live under the poverty line, with 37% living in extreme poverty (4). Rwanda's GDP (nominal) is ranked number 141 of 190 by the World Bank (3). Currently, there are 41 district hospitals and 400 health centers with 0.05 physicians and 0.42 nurses per 1000 citizens (5). The country now utilizes a community-based health insurance system named Mutuelle de Sante which allows even the poorest citizens access to needed care (6). Specialist diabetes

care is often not available, however, and is centered mainly at the Association Rwandaise des Diabetiques (ARD) in the capital, Kigali and a few specific hospitals developed by Partners in Health. A team from the ARD attempts to visit approximately half the district hospitals on a quarterly basis.

Due to the paucity of available trained diabetes professionals and supplies, outside help has been vital. One such program is the International Diabetes Federation's Life For a Child (LFAC) program, which is managed in conjunction with Australian Diabetes Council and HOPE*worldwide*. LFAC's mission is to support the provision of the best possible health care, given local circumstances, to all children and young adults (≤25 yr) with diabetes in lower-income countries, through the strengthening of youth diabetes services in these countries. This is done through the provision of insulin, syringes, glucose monitoring supplies, diabetes education and training. This program works with the ARD in Rwanda to address the emerging diabetes problem. Children and adolescents who are supported by this program have an annual LFAC form completed, which collects basic clinical and laboratory measures. The University of Pittsburgh Graduate School of Public Health also supports this program and annually sends a MPH student to help with completing the assessments.

Since there are currently very few observational studies on diabetes in Africa (7–12), especially those focusing specifically on type 1 diabetes (T1D) in youth, we present data on a cohort of Rwandan adolescents and children with T1D, using data collected for the LFAC program for 2009 and 2010. The objectives of this report are, first, to describe the current clinical status of the program participants and second, to identify factors which may relate to level of glycemic control (HbA1c) and complication status, in order to facilitate and prioritize management.

Methods

This report concerns a quality improvement project of the LFAC Program in collaboration with the ARD and The University of Pittsburgh Graduate School of Public Health. The University of Pittsburgh's IRB has determined that this project is exempt from review under the 'Existing Data' category.

Study population

All participants of this program evaluation are registered participants of the Rwanda LFAC program. To be enrolled in the program, the participant must be a Rwandan citizen aged 25 yr and younger and need assistance with obtaining insulin and/or other diabetes supplies. Participants either sought out care directly from the ARD or were referred there by their physicians or other healthcare providers. Due to uncertainty about month of birth for two participants, they were included though they may have been aged 26 yr.

Data collection

Data collection occurred between June 2009 and November 2010. Most data were collected during two 6-wk periods (June–July 2009 and May–June 2010) and comprise of data from patients' first HbA1c reading. Two University of Pittsburgh MPH students [SM (2009) and VS (2010)] assisted the ARD staff in this process. Additional baseline data for individuals who had their first HbA1c through November 2010, are also included. In n = 78 cases, the HbA1c reading was on first entry into LFAC.

The LFAC forms and protocol were used to collect data at the ARD and several regional hospitals that the program supports (2009 – Kigeme, Gisheme, Nemba, Gisenyi, and Kabgayi; 2010 – Kigeme, Kabgayi, Butare, Kilinda, Gisenyi, and Kibungo). Medical history and clinical examinations lasted an average of 30 min and were facilitated by a translator/nurse from the ARD staff. All assisting University of Pittsburgh students and ARD clinical staff were trained by T. O. and D. E.

No data were collected for research purposes and all data reported are routine clinical data recorded for clinical program purposes.

LFAC annual forms. The LFAC program has developed a clinical history and exam data form to be completed annually for each youth supported with insulin through LFAC. These forms include: date of birth, date of diagnosis, number of injections per day, units of insulin per day, type of insulin used, average number of visits to a doctor/clinic per yr, height, weight, blood pressure (BP), neuropathy assessment (monofilament and tuning fork tests), HbA1c, Albumin – Creatinine ratio (A/C ratio), number of hypoglycemic episodes, number of hospitalizations, and school attendance (for those of school going age – 4–23 yr, N = 252).

LFAC quarterly review forms. A quarterly review system was developed to allow the ARD staff to better monitor the children receiving supplies from the LFAC program and allow for more accurate and timely adjustments to their insulin regimens. These forms include information on: number of glucose measurements per week, a random glucose measure, number of insulin injections per day, total number of insulin units, height, weight, BP, HbA1c, and A/C ratio (A/C information was only collected for

quarterly review if the value was >30 mg/g at the annual assessment).

Laboratory data. Blood (finger prick) and urine (spot samples) were collected from each patient and processed on the Siemens DCA Vantage™ (Tarrytown, NY, USA) (which reports DCCT equivalent units) by MPH students or ARD staff. Data for HbA1c and A/C ratio were collected from these samples. HbA1c and A/C ratio results were reported to the nearest tenth. The maximum HbA1c value for this machine is '>14% (>130 mmol/mol),' so for data analysis purposes these results were reported as '14.1% (131 mmol/mol).' The CV range for the DCA was 2.1–3.8% during the data collection.

Complication assessment

Neuropathy. Neuropathy was assessed though use of monofilament and 128 Hz tuning fork tests. The monofilament was applied a total of ten times to the dorsum of the great toe. At least 7 correct responses of 10 applications were considered to be a normal result (13).

The vibrating tuning fork was placed on the dorsum of the great toe, and the test was considered abnormal if the patient indicated they could no longer feel the vibrations within 10 s (13). Neuropathy was then defined as either/or both an abnormal monofilament *or* abnormal tuning fork result.

Microalbuminuria/nephropathy. Microalbuminuria (MA) was defined as an albumin/creatinine (A/C) ratio of 30–299 mg/g in a spot urine sample, and overt nephropathy as an A/C ratio greater than or equal to 300 mg/g.

Hypertension. Hypertension was defined as having systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥80 mmHg or a history of BP medication.

Data analysis

Descriptive statistics including mean, median, standard deviation, and frequencies were calculated for all variables. Two-sample t-tests and ANOVAs were used to assess difference among continuous variables, and the chi-squared test for differences among categorical variables. Tukey's HSD test was used for any post-hoc pairwise comparisons. While a nominal p-value of $p < 0.05$ is used to denote significance, given the multiple comparisons in Tables 1, 2, and 4, a Bonferroni corrected p-value of $p < 0.002$ is indicated as a footnote for assessment purposes.

Due to the high proportion (30.8%) of patients with HbA1c >14.0% (130 mmol/mol), we decided to examine HbA1c in two ways. The first was to group those with HbA1c >14% (130 mmol/mol) together and label them as having 'poor control' and then divide the rest into two groups: 'better control [<8.0% (<64 mmol/mol)]', and 'intermediate control [8.1–14.0% (65–130 mmol/mol)].' The second approach was to separate out those with HbA1c >14% (130 mmol/mol), and then treat HbA1c as a continuous variable.

Multiple linear regression modeling was used to identify factors that predict the continuous HbA1c variable. Univariate associations were first examined to identify possible predictors and those with significance of $p \leq 0.2$ were then considered for inclusion in the final model. Backwards stepwise regression was then completed using a significance of $p < 0.05$ for inclusion. Age was retained as a potential confounder.

A similar process was used for development of a logistic regression model for MA. Age was also retained as a potential confounder. The analysis for this article was generated using SAS/STAT software, Version 9.3 of the SAS System for Windows, copyright © 2011 SAS Institute Inc.

Results

Current clinical status

From June 2009 to November 2010, a total of 301 LFAC children and youth had their first recorded HbA1c test. Fifteen of these children were not regularly taking insulin, and were therefore excluded from further analysis, resulting in a final cohort of 286 youth and adolescents. Their mean age was 18.6 ± 4.5 yr (range 0–26 yr), duration 3.4 ± 3.1 yr (range 0–17 yr), and age of diagnosis was 15.1 ± 4.8 yr (range 0–26 yr). The vast majority (83.1%, n = 236) checked blood glucose once or less per week, however, 91.0% (n = 192) were able to visit a clinic for diabetes care at least once per month. Mean body mass index (BMI) was 20.2 ± 4.0 kg/m^2 and 35.7% (n = 100) had documented hypertension. The mean HbA1c for this cohort was 11.2 ± 2.7% (99 ± 30 mmol/mol) with 45 patients (15.7%) having HbA1c under 8% (64 mmol/mol), and 88 (30.8%) with HbA1c over 14% (130 mmol/mol). Only 3.8% (n = 11) participants reported any use of analog insulin, while 96.1% (n = 275) were using NPH/regular and Lente insulin.

Only 51.4% (n = 108) of participants of school going age were attending school, and of those 63.9% were in the wrong grade for their age. Diabetes was reported as limiting school attendance in some way for 40.5% (n = 85) of children.

The male to female ratio for the overall cohort is 1:1.15 – a slight female preponderance (Table 1). The

Table 1. Demographic data for the 2009–2010 Rwanda LFAC Cohort, by sex

	Males		Females		
	N	Mean	N	Mean	p
Age (yr)	133	19.0 ± 4.5	153	18.3 ± 4.5	0.182
Diagnosis age (yr)	131	15.7 ± 5.0	150	14.6 ± 4.6	0.050
Duration (yr)	131	3.2 ± 2.8	150	3.5 ± 3.4	0.381
Monitoring/wk	132	1.1 ± 3.1	152	1.3 ± 3.7	0.865
Insulin Units/kg	125	0.75 ± 0.34	144	0.71 ± 0.38	0.284
Visits/yr	98	15 ± 13	113	14 ± 12	0.556
Weight (kg)	128	48.7 ± 12.9	151	47.6 ± 12.6	0.472
Height (cm)†	127	156.9 ± 16.5	148	151.8 ± 12.2	<0.001*
BMI (kg/m^2)†	125	19.4 ± 4.0	146	20.8 ± 3.0	0.002*
Systolic BP (mmHg)†	130	113 ± 14	150	111 ± 15	0.136
Diastolic BP (mmHg)†	130	72 ± 10	150	73 ± 11	0.291
HbA1c (%)	133	11.5 ± 2.6	153	11.0 ± 2.7	0.084
HbA1c (mmol/mol)	133	102 ± 29	153	96 ± 30	0.084
A/C	60	44.5 ± 108.7	89	55.9 ± 139.9	0.595
Province	133	—	153	—	0.096
North		9.8 (13)		16.3 (25)	
South		36.8 (49)		34.6 (53)	
East		12.0 (16)		10.5 (16)	
West		17.3 (23)		8.5 (13)	
Kigali City		24.1 (32)		30.1 (46)	
Live in urban area	133	23.3 (31)	153	30.1 (46)	0.199
Monitor ≤1/wk	132	84.1 (111)	152	82.2 (125)	0.678
Attending school	90	45.5 (41)	120	55.8 (67)	0.164
In correct grade for age	40	35.0 (14)	67	35.8 (24)	0.932
Attendance limited by diabetes	76	50.0 (38)	102	46.1 (48)	0.650
Hypertension	130	36.9 (48)	150	34.7 (52)	0.71
Neuropathy	106	1.9 (2)	130	2.3 (3)	1.000
Microalbuminuria	60	16.7 (10)	89	23.6 (21)	0.307
Nephropathy	60	5.0 (3)	89	4.5 (4)	1.000

BP, blood pressure; BMI, body mass index; LFAC, Life For A Child.
N and Mean ± SD, are presented for all continuous variables, while % (n) are reported for categorical variables and outcomes. p values for two-sample t-tests are presented for continuous variables and either chi-squared or Fisher's exact (based on cell numbers) are presented for categorical data. The corresponding Bonferroni corrected p-value is $p < 0.002$.
*Denotes $p < 0.05$.
†Denotes that the variable was controlled for sex and age.

distribution of age at diagnosis for both sexes was similar with a borderline later mean age at diagnosis for boys (15.7 ± 5.0 yr) than females (14.6 ± 4.6 yr, p = 0.05) (Table 1 and Fig. 1). Males had higher mean height (156.9 ± 16.5 cm vs. 151.8 ± 12.2 cm, $p < 0.001$) and females, had higher mean BMI (20.8 ± 3.0 kg/m^2 vs. 19.4 ± 4.0 kg/m^2, p = 0.003). The difference in mean HbA1c between sexes (11.5 ± 2.6% (102 ± 29mmol/mol) for males, 11.0 ± 2.7% (96 ± 30 mmol/mol) for females) approached significance (p = 0.084).

The urban to rural ratio for this cohort was 1:2.7, with significantly more people living in rural areas than urban. Patients living in urban areas had higher mean height (159.3 ± 1.38 cm vs. 152.2 ± 0.84 cm, $p < 0.001$) and systolic blood pressure (116.6 ± 1.6 mmHg vs. 110.9 ± 0.9 mmHg, p = 0.002) than those living in rural areas, after controlling for age and gender.

A total of 83.1% (n = 236) patients measured their glucose levels once or less per week. Mean age (16.6 ± 0.6 yr vs. 19.1 ± 0.3 yr, p = 0.003) and age at diagnosis (12.2 ± 0.7 yr vs. 15.8 ± 0.3 yr, $p < 0.001$) was lower for those who monitored only once or less a week as compared to those who monitor more frequently. Duration was longer (4.4 ± 3.5 yr vs. 3.2 ± 3.0 yr, p = 0.015) for those who monitored once or less a week, after adjusting for age.

HbA1c control

Those with 'better control' were more likely to have a shorter duration (2.1 ± 2.5 yr) than the 'intermediate control' (p = 0.001), but not the 'poor control' group (p = 0.2) (Table 2). The 'better control' group had a similar insulin dose per kg (0.61 ± 0.28 units/kg) with the 'intermediate control' group (p = 0.18), but lower than those in the 'poor control' group (p = 0.019). In contrast, the 'poor control' group had significantly lower systolic BP (108 ± 14 mmHg) than those in the 'intermediate' (p = 0.01) and 'better' (p = 0.01) control

Table 2. Clinical data for the 2009–2010 Rwanda LFAC Cohort, by HbA1c grouping

	'Better control'<8.0%		'Intermediate control'8.1–14.0%		'Poor control'>14.0%		
	N	Mean	N	Mean	N	Mean	p
Age (yr)	45	18.8 ± 4.2	152	18.7 ± 4.8	88	18.3 ± 4.2	0.786
Diagnosis age (yr)	44	16.6 ± 3.7	149	14.6 ± 5.1	88	15.3 ± 4.7	0.053
Duration (yr)	44	2.1 ± 2.5	149	4.0 ± 3.3	88	3.0 ± 2.9	0.001*
Monitoring/wk	45	1.2 ± 4.7	152	1.2 ± 3.5	87	0.81 ± 2.4	0.633
Insulin units/kg	41	0.61 ± 0.28	143	0.72 ± 0.31	85	0.80 ± 0.46	0.025*
Visits/yr	33	16 ± 17	112	14 ± 10	66	15 ± 14	0.760
Weight (kg)	44	50.1 ± 11.7	148	48.5 ± 13.1	87	46.3 ± 12.5	0.216
Height (cm)†	44	153.6 ± 13.8	146	154.2 ± 15.2	85	154.3 ± 14.6	0.828
BMI (kg/m^2)†	43	21.0 ± 4.9	143	20.2 ± 3.9	85	19.7 ± 3.4	0.065
Systolic BP (mmHg)†	45	115 ± 11	150	113 ± 16	85	108 ± 14	0.005*
Diastolic BP (mmHg)†	45	72 ± 11	150	74 ± 11	85	70 ± 11	0.031*
HbA1c (%)	45	6.6 ± 1.0	153	10.9 ± 1.5	88	14.1	<0.001*
HbA1c (mmol/mol)	45	49 ± 11	153	96 ± 16	88	131	<0.001*
A/C	14	12.0 ± 8.3	83	51.4 ± 128.7	52	61.7 ± 142.6	0.439
Males	45	33.3 (15)	153	47.7 (73)	88	51.1 (45)	0.136
Province	45	—	153	—	88	—	0.179
North		14.8 (8)		11.8 (18)		13.7 (12)	
South		46.7 (21)		35.3 (54)		30.7 (27)	
East		11.1 (5)		10.4 (16)		12.5 (11)	
West		6.7 (3)		10.4 (16)		19.3 (17)	
Kigali City		14.8 (8)		32.0 (49)		23.9 (21)	
Live in Urban Area	45	14.8 (8)	153	31.4 (48)	88	23.9 (21)	0.144
Monitor ≤1/wk	45	86.7 (39)	152	80.9 (123)	87	85.0 (74)	0.560
Attending school	35	54.3 (19)	108	50.9 (55)	65	52.3 (34)	0.939
In correct grade for age	19	42.1 (8)	55	41.8 (23)	33	21.2 (7)	0.119
Attendance limited by diabetes	31	35.5 (11)	94	51.1 (48)	53	49.0 (26)	0.314
Hypertension	45	28.9 (13)	150	40.7 (61)	85	30.6 (26)	0.17
Neuropathy	42	4.8 (2)	124	1.6 (2)	70	1.4 (1)	0.421
Microalbuminuria	14	0.0 (0)	83	22.9 (19)	52	23.1 (12)	0.131
Nephropathy	14	0.0 (0)	83	4.8 (4)	52	5.8 (3)	0.662

BP, blood pressure; BMI, body mass index; LFAC, Life For A Child.
N, and Mean ± SD, are presented for all continuous variables, while % (n) are reported for categorical variables. p values for ANOVA are presented for continuous variables and either chi-squared or Fisher's exact (based on cell numbers) are presented for categorical data. The corresponding Bonferroni corrected p-value is $p < 0.002$.
*Denotes $p < 0.05$.
†Denotes that the variable was controlled for sex and age.

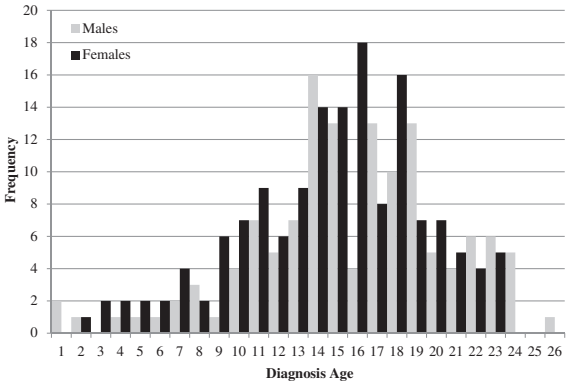

Fig. 1. Age at diagnosis of diabetes by sex for the 2009–2010 Life For A Child cohort.

groups. Those in the 'poor control' group also had lower diastolic BP (70 ± 11 mmHg) than those in the 'intermediate control' ($p = 0.01$), but were similar to those in the 'better control' group ($p = 0.82$).

We then compared those who have 'poor control' [HbA1c >14.0% (>130 mmol/mol)] to those under 14% (130 mmol/mol) (data not shown). Only units of insulin/kg and systolic BP differed significantly. People with HbA1c >14% (>130 mmol/mol) had higher reported units of insulin/kg (0.80 ± 0.04 vs. 0.70 ± 0.03, $p = 0.04$) and had lower systolic BP (107.9 ± 1.6 mmHg vs. 114 ± 1.1 mmHg, $p = 0.001$).

In the final linear regression model, duration, units of insulin per kg, and living in the Southern Province were significantly associated with HbA1c, after adjusting for each factor and age (Table 3). A 1-yr longer disease duration was associated with a 0.18% ($p < 0.001$) greater HbA1c, and a 0.1 unit/kg greater insulin dose was associated with a 0.17% greater HbA1c ($p = 0.002$), after adjusting for age and province. Living in the southern province was associated with a 0.82% lower HbA1c, after adjusting for age, duration and units/kg of insulin.

Table 3. Point estimates of differences in HbA1c from multiple linear regression model for those with HbA1c under 14%, in the 2009–2010 Rwanda LFAC cohort. Age was retained as a potential confounder

	Coefficient	p
Age (yr)	0.0001	0.90
Duration (yr)	0.184	<0.001*
Units of insulin/kg	1.68	0.002*
Southern Province	−0.817	0.013*

*Denotes $p < 0.05$.

Complications

Thirty-one (21%) children and youth had MA. Those with MA had younger mean age at diagnosis (17.9 ± 4.2 yr vs. 18.9 ± 4.3 yr, $p = 0.01$) and longer disease duration (5.0 ± 3.1 yr vs. 3.5 ± 3.2 yr, $p = 0.02$) than those without MA (Table A1). MA patients also had lower mean weight (45.5 ± 11.0 kg vs. 50.5 ± 12.5 kg, $p = 0.048$) than those without, even after adjusting for age. Diastolic blood pressure was also higher in those with MA (77 ± 13 mmHg vs. 71 ± 11 mmHg, $p = 0.02$). Although HbA1c was not significantly different ($p = 0.16$), the mean HbA1c was 0.7% higher for those with MA.

Five percent ($n = 7$) of participants had overt nephropathy; five of which had a diabetes duration <10 yr. There were no differences for any variables between those who have nephropathy and those who do not (Table A1).

Five (2.1%) participants had either abnormal tuning fork vibratory sensation or monofilament response. Those with neuropathy had higher mean age (23.0 ± 1.6 yr vs. 18.6 ± 4.2 yr, $p = 0.02$) than those who did not have neuropathy (Table A1). Hypertension was present in three patients, and another had concomitant MA.

Complications were not assessed for everyone due to the staged introduction of these exams and logistical issues. Since the number of cases for neuropathy and nephropathy were so low, only MA was modeled multivariably. One year of additional disease duration significantly increased the odds of having MA by 1.19 (95% CI, 1.05–1.36), after adjusting for other predictors (Table 4). Older age [OR 0.86 (95% CI, 0.77–0.96)] had a protective effect, while increases in diastolic blood pressure [OR 1.07 (95% CI, 1.02–1.11)] and HbA1c [OR 1.24 (95% CI, 1.01–1.53)] increased the odds of MA. However, in a subgroup analysis of those of school going age (ages 4–23 yr), school attendance is borderline predictive of MA (2.92 [95% CI, 0.99–8.6] $p = 0.05$), and age is no longer significant ($p = 0.8$).

Table 4. Final, multivariable logistic models for microalbuminuria in the 2009–2010 LFAC Cohort. Two models are presented, the first is for the entire cohort (A), and the second is only for those of school age (B). The reference intervals for OR estimation are per unit of measure

	OR (95% CI)	p
A. Overall		
Age (yr)	0.86 (0.77–0.96)	0.009*
Duration (yr)	1.19 (1.05–1.36)	0.008*
Diastolic BP (mmHg)	1.07 (1.02–1.11)	0.004*
HbA1c (%)	1.24 (1.01–1.53)	0.047*
B. School age (4–23 yr)		
Age (yr)	0.88 (0.77–1.08)	0.800
Duration (yr)	1.24 (1.07–1.45)	0.005*
Diastolic BP (mmHg)	1.09 (1.03–1.14)	0.001*
HbA1c (%)	1.26 (1.0–1.60)	0.050
Attending school (yes/no)	2.92 (0.99–8.6)	0.052

BP, blood pressure.
*Denotes $p < 0.05$.

Discussion

The youth in this LFAC program were clearly in very poor glycemic control as mean HbA1c was $11.2 \pm 2.7\%$ (99 ± 30 mmol/mol), and 30.8% ($n = 88$) had an HbA1c over 14% (130 mmol/mol). Mean age of participants was 18.6 ± 4.5 yr and mean duration of disease was 3.4 ± 3.1 yr. Most of the children (83.1%, $n = 236$) were unable to check their glucose more than once per week, and several of the children and youth had already presented with complications. The vast majority of clinic visits are mainly to collect insulin, however, regimen adjustments may also be made at this time. This approach minimizes the need for home refrigeration and is also often necessary due to limited supplies of insulin.

The rates of MA, nephropathy, and neuropathy were 20.8, 4.7, and 2.1%, respectively. These rates are similar to those in Kinshasa, Congo, where rates of MA and nephropathy of 21.9 and 7.3%, respectively, were found in a cohort with mean age 19.1 ± 5.8 yr and disease duration of 57.6 ± 45.1 months (4.8 ± 3.8 yr) (14). In an additional cohort from Tanzania with mean age 12.6 ± 3.5 yr and diabetes duration of 4.76 ± 3.58 yr, 29.3% had MA (9).

There are more females in our population than males. While this has also been seen in some other African populations such as Tanzania (11, 9), Libya (15), and Nigeria (16) there is more often a male predominance [Tunisia (17), Cameroon (18), Ethiopia (19), and Nigeria (20)]. In our population, males were diagnosed at an older age than females (15.9 ± 5.1 yr vs. 14.8 ± 4.7 yr), as is consistent with other African and non-African populations (10, 12). Compared to developed countries, the mean age of presentation in Rwanda is older, which is consistent with other African populations (7, 21–24). This pattern, however,

raises concerns about the potential for missed cases at younger ages that were fatal before proper diagnosis was made.

The effects of this disease are not only reflected in the rates of complications, but are also manifested in the reduced rates of school attendance. With only 36.1% of those of school going age in the correct grade for their age, and 40.5% reporting some limitation in school attendance due to diabetes, it is clear that this disease is affecting many facets of these children's and youths' lives. Unfortunately, since grade was not recorded, we are unable to make a direct comparison to the Rwanda general population.

Additionally, there are no data for age and sex specific BMI in Rwanda. However, the Demographic and Health Survey for 2005 (25) does report that 17% of women age 15–19 have a BMI $<18.5\,kg/m^2$. This compares to 21.3% (n = 13/61) in our population. So we conclude that while our population is lean, it does not differ significantly from the general population for this age/sex subgroup.

The urban to rural ratio for our population was higher than that of the general population [1:2.7 vs. 1:4.3 (26)]. The higher ratio seen in our population may be due to limited resources for diabetes diagnosis and management in rural areas and the urban location of the clinic.

HbA1c control

Disease duration, systolic and diastolic blood pressure, and units of insulin per kg, were identified as factors that differed by HbA1c control groups. When HbA1c was analyzed as a continuous variable, longer disease duration, more units of insulin per kg, and living in a province other than the Southern province were predictive of increases in HbA1c%, in a multivariable model.

Longer disease duration has previously been associated with poorer glucose control (27). A cohort in Sudan, however, found an opposite relationship between duration and HbA1c, though they attributed it to low patient survival and poor compliance with management in younger children with shorter disease duration (28). Those with 'better control' in our cohort, required lower doses of insulin/kg, suggesting that there may still be residual β-cell function, which is consistent with the shorter disease duration in this group (29). Additionally, it is possible that there are people in this group who have a non-traditional form of diabetes. Studies in Ethiopia and Cameroon (18, 30, 31) have suggested a different type of diabetes present in African populations that requires less, and non-continuous, use of insulin. Since, no typology tests have yet been performed in this cohort, we have no way of definitively diagnosing T1D or any alternative forms. Systolic BP is highest in the 'better control' group, however, this may be a reflection of better overall health as compared to those with 'poor control'. The lower systolic BP in the 'poorer control' groups may be due to malnutrition and hypovolemia due to dehydration, which is consistent with the lower BMI and diastolic BP seen in the 'poor control' group (32). Diastolic BP was highest in the 'intermediate control' group and may be due to the fact that higher diastolic BP has been previously shown to be associated with poor glycemic control (33).

Those living in the Southern Province may have lower HbA1c due to a higher level of care available at the local hospital. The main hospital (Kabgayi) is located very close to Kigali (~28 miles) and the ARD, and the nurses that provide care at the hospital are well organized and educated. They are also skilled at sharing their knowledge with their patients.

Frequency of monitoring does not predict HbA1c; however, there were only three patients in this cohort who monitored the suggested three times per day (34). Therefore due to the low frequency of testing in this population, the true benefits of frequent testing may not be measurable. Additional efforts should be made to enable the patients to measure their glucose more frequently and adjust diet and/or insulin accordingly. Current efforts of the LFAC program are focused on this objective.

Complications

In the final multivariable logistic regression model, duration, diastolic blood pressure, and HbA1c were positive predictors for MA, while increased age was protective. This effect of age may reflect a somewhat less severe disease in the older youth or even a survivor effect. The higher risk of MA in those of school going age who are attending school is intriguing. Children and youth attending school in this cohort have expressed trouble with being allowed access to insulin and testing supplies during the school day, which may lead to compromised management, and increased risk.

None of the patients in the 'better control' group had MA, supporting the idea that good glucose control reduces the risk of developing MA in youth and adolescents (35–37).

Duration is a well-established risk factor for MA (36–38). Higher diastolic BP was also associated with MA, which is consistent with some, but not all prior research, suggesting BP elevation is an important risk factor for MA (37, 39). The clear association in this population, however, suggests that it is truly a risk factor for, and not a consequence of, MA. Increased BP has also been previously identified as a risk factor for MA in African populations (28). More frequent clinic visits and earlier blood pressure control may

allow the patient to receive more adequate prevention of MA.

Although the overall rate of complications is still low in this population it is of note, that the mean duration for each of these complications is well under 10 yr, indicating a rapid development of complications, at least for some individuals. This is likely to be due to very poor glucose control in this cohort and possibly also a delayed diagnosis and initiation of treatment. This will be more fully explored in future studies.

Strengths and limitations

This is the first observational study of a cohort of children and adolescents with T1D in Rwanda and we feel is fairly representative of known childhood diabetes in Rwanda, given the limited access to insulin. However, since this is not a complete country registry for T1D, these data may not be representative of the entire Rwandan diabetic community. It is also likely that there are children and adolescents who die before diagnosis, which could cause an underrepresentation of the true magnitude of the problem. Misdiagnosis is also possible in developing countries such as this, as a previous study in Tanzania found that 21 of 199 patients diagnosed with cerebral malaria actually had coma due to uncontrolled diabetes (40).

Our complication assessment was limited due to lack of diagnostic tools for retinopathy and because MA and nephropathy were assessed using a single urine sample. Our analysis was further complicated by incomplete clinical data and complication status assessment. Limited reagents and because complications were only assessed on the LFAC Annual form (not the Quarterly), were the main reasons as to why complication status was not fully assessed. We have no reason to believe that this introduced any systematic bias. Pubertal stage was not recorded in this study. However, as this could provide additional information on metabolic control, the effects of complications, insulin dose, and growth, we suggest that this data be recorded in the future if possible. This study is also limited in that it is of cross sectional design, thus limiting our measures to those of association rather than true prediction.

Conclusions

These data from the LFAC program for 2009–2010 show that there is a great need for dramatically improved care, as many patients have greatly elevated HbA1c measures, often >14%. However, with the greater availability of insulin, blood testing supplies, education and a more formal quarterly clinical review process in place, we believe the ARD staff, patients, and their families will be better positioned to make appropriate and timely adjustments to their patients' treatment regimens. These data have identified correlates of better control (e.g., living in the Southern province) and MA (e.g., diastolic blood pressure), both of which provide potential avenues to improved quality of care.

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Appendix

Table A1. Clinical data for the 2009–2010 LFAC Cohort by complication status

Status	Microalbuminuria			Nephropathy			Neuropathy		
	Yes (n = 31)	No (n = 118)	p	Yes (n = 7)	No (n = 142)	p	Yes (n = 5)	No (n = 231)	p
Age (yr)	17.9 ± 4.2	18.9 ± 4.3	0.237	20.0 ± 3.9	18.6 ± 4.3	0.407	23.0 ± 1.6	18.6 ± 4.2	0.020*
Diagnosis age (yr)	12.9 ± 3.9	15.3 ± 4.8	0.011*	12.6 ± 3.8	14.9 ± 4.8	0.210	17.0 ± 3.8	15.1 ± 4.8	0.378
Duration (yr)	5.0 ± 3.1	3.5 ± 3.2	0.024*	7.4 ± 5.9	3.7 ± 2.9	0.144	6.0 ± 3.3	3.5 ± 3.2	0.078
Monitoring/wk	1.1 ± 3.8	1.3 ± 3.8	0.786	1.6 ± 2.6	1.3 ± 3.8	0.843	3.4 ± 6.0	1.1 ± 3.6	0.156
Injections/day	1.8 ± 0.6	1.9 ± 0.7	0.357	2.0 ± 0.0	1.9 ± 0.7	0.594	1.6 ± 0.5	1.8 ± 0.6	0.364
Units/kg	0.71 ± 0.3	0.70 ± 0.4	0.875	0.86 ± 0.3	0.70 ± 0.4	0.267	0.45 ± 0.1	0.71 ± 0.4	0.096
Visits/yr	12.0 ± 10.0	15.8 ± 14.1	0.214	16.8 ± 6.6	14.8 ± 13.5	0.737	10.5 ± 3.0	14.9 ± 12.8	0.493
Weight (kg)	45.5 ± 11.0	50.5 ± 12.5	0.048*	51.0 ± 17.3	49.4 ± 12.1	0.734	56.4 ± 12.3	48.0 ± 12.3	0.131
Height (cm)†	153.7 ± 14.6	154.7 ± 14.2	0.710	154.6 ± 12.2	152.6 ± 14.6	0.680	149.2 ± 14.1	153.7 ± 14.7	0.430
BMI (kg/m^2)†	19.9 ± 3.4	20.8 ± 4.1	0.210	20.4 ± 4.6	20.7 ± 4.0	0840	21.6 ± 5.0	20.2 ± 4.2	0.440
Systolic BP (mmHg)†	114 ± 20	111 ± 15	0.290	115 ± 8	111 ± 17	0.550	111 ± 15	111 ± 15	0.730
Diastolic BP (mmHg)†	77 ± 12	71 ± 11	0.010*	72 ± 8	73 ± 11	0.890	76 ± 14	72 ± 11	0.530
HbA1c (%)	12.3 ± 1.9	11.6 ± 2.4	0.165	12.1 ± 2.0	11.8 ± 2.3	0.736	10.2 ± 2.7	11.1 ± 2.8	0.450
HbA1c (mmol/mol)	111 ± 21	104 ± 26	0.165	108 ± 22	105 ± 26	0.736	88 ± 29	98 ± 30	0.450
A/C	76.1 ± 58.7	44.8 ± 140	0.227	559.8 ± 229	26.2 ± 38.5	<0.001	36.7 ± 44.8	49.9 ± 113	0.797
Male	32.2 (10)	42.4 (50)	0.307	42.8 (3)	40.1 (57)	1.000	40.0 (2)	45.0 (104)	1.000
Province	—	—	0.93	—	—	0.55	—	—	0.52
North	16.0 (4)	84.0 (21)	4	4.0 (1)	96.0 (2)	0	2.8 (1)	97.2 (35)	3
South	20.0 (7)	80.0 (28)		0.0 (0)	100 (35)		0.0 (0)	100 (89)	
East	18.2 (2)	81.8 (9)		9.1 (1)	91.0 (10)		4.0 (1)	96.0 (24)	
West	26.1 (6)	73.9 (17)		4.3 (1)	95.6 (22)		3.3 (1)	96.7 (29)	
Kigali City	21.8 (12)	78.2 (43)		7.3 (4)	92.7 (51)		3.6 (2)	96.4 (54)	
Live in urban area	38.7 (12)	36.4 (43)	0.816	57.1 (4)	35.9 (51)	0.424	4.0. (2)	23.4 (54)	0.340
Monitor ≤1/wk	83.9 (26)	75.2 (88)	0.308	35.9 (4)	78 (110)	0.198	60.0 (3)	84.3 (194)	0.185
Attending school	72.4 (21)	52.5 (42)	0.063	50.0 (2)	58.5 (62)	0.735	52.5 (104)	0.0 (0)	0.071
In correct grade for age	23.8 (5)	30.9 (13)	0.554	100.0 (2)	25.8 (16)	0.407	35.9 (37)	0.0 (0)	0.198
Attendance limited by diabetes	64.3 (18)	43.8 (35)	0.061	75.0 (3)	48.1 (104)	0.291	46.7 (79)	66.7 (2)	0.493
Hypertension	41.9 (13)	34.8 (40)	0.460	42.9 (3)	36.0 (50)	0.710	60.0 (3)	33.3 (76)	0.210
Neuropathy	3.3 (1)	4.4 (4)	1.000	0.0 (0)	4.3 (5)	1.000	—	—	—
Microalbuminuria	—	—	—	0.0 (0)	21.8 (31)	0.346	20.0 (1)	25.2 (29)	1.000
Nephropathy	0.0 (0)	5.9 (7)	0.346	—	—	—	0.0 (0)	4.3 (5)	1.000

BP, blood pressure; BMI, body mass index; LFAC, Life For A Child.
Mean±SD are presented for all continuous variables, while % (n) are reported for categorical variables and outcomes. p values for two-sample t-tests are presented for continuous variables and either chi-squared or Fisher's exact (based on cell numbers) are presented for categorical data. The appropriate Bonferroni corrected p-value is $p < 0.002$.
*Denotes $p < 0.05$.
†Denotes that the variable was controlled for sex and age.