Survey on Acute and Chronic Complications in Children and Adolescents With Type 1 Diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania

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OBJECTIVE — The purpose of this study was to assess glycemic control and complications of type 1 diabetes in children and adolescents in Tanzania.

RESEARCH DESIGN AND METHODS — This demographic and clinical survey included 99 children aged between 5 and 18 years attending Muhimbili National Hospital Clinic for Diabetes. A structured questionnaire was used for evaluating socioeconomic data and for estimation of the prevalence of acute complications occurring over the last 6 months. The prevalences of retinopathy and diabetic nephropathy were determined by fundus ophthalmoscopy and by microalbuminuria, respectively.

RESULTS — All of these children were treated with a conventional insulin regimen. The mean ± SD duration of diabetes was 4.76 ± 3.58 years. Only 1 child (1%) had good glycemic control (A1C <7.5%), 60 children (60.6%) had moderate glycemic control (A1C 7.5–10%), 14 children (14.1%) had poor glycemic control (A1C >10–12.5%), and 24 children (24.2%) had very poor glycemic control (A1C >12.5%). At onset of diabetes, 75% of children presented with diabetic ketoacidosis (DKA); 89 children (89.80%) had at least one episode of DKA, and 55 children (55.67%) had symptomatic hypoglycemic episodes. Microalbuminuria was present in 29 (29.3%) and retinopathy in 22 (22.68%) children.

CONCLUSIONS — Although there are some methodological limitations, this survey highlights the difficulties of achieving good metabolic control and the high prevalence of acute and chronic complications in Tanzanian children with type 1 diabetes. These results clearly show that major efforts are needed to improve quality of care in children with type 1 diabetes in Tanzania.

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Type 1 diabetes is one of the most frequent chronic disease in children and represents a public health challenge globally. Its burden is huge in developing countries owing to the lack of a basic means for reaching reasonable glycemic control. Because of the unavailability of reliable epidemiological data, the natural history of type 1 diabetes, including its complications, is largely unknown (1). With the few data available on sub-Saharan African children, incidence in Tanzania was estimated to be 1.5/100,000 (2), and an increase in incidence in Sudan from 9.5/100,000 in 1991 to 10.3/100,000 in 1995 has been reported (3). The prevalence is higher in Western countries (4,5), suggesting the possibility of missed diagnosis in sub-Saharan Africa. In fact, the problem of missed diagnosis of childhood diabetes, although not unique to developing countries (6), is certainly much more common than in developed countries (7). In a Sudanese study, it was reported that 10% of children were not admitted at the time of diagnosis, being admitted only after they developed diabetic ketoacidosis (DKA) or hypoglycemia (3). This situation contributes to omission of patients in the registry as well as to the possibility of death before diagnosis, especially for those aged <5 years. In sub-Saharan Africa, most children present with DKA at the time of diagnosis (8,9), which could easily be misdiagnosed as cerebral malaria or meningitis in the busy emergency reception areas of most hospitals in Africa (7). Poor facilities in most of these countries may also contribute to death before diagnosis. The precipitating factors for DKA in sub-Saharan Africa are mainly newly diagnosed diabetes, missed insulin doses, and infections (10). In the developed world, enormous efforts are made to reduce the chronic complications of diabetes, yet in the developing world, the incidence of these complications in children is not known, making their management more difficult.

Information on chronic complications of diabetes in sub-Saharan Africa is scarce; however, the incidence has gone hand in hand with the growing disease prevalence, demonstrating the importance of assessing complications. The few studies on chronic complications of diabetes in sub-Saharan Africa included type 1 and 2 adult diabetic patients (11,12). The only study evaluating both adult and children reported a 14% prevalence of retinopathy and a 7.5% prevalence of nephropathy (13). Because there have been no data to date on the complications of type 1 diabetes in children in Tanzania, we performed a hospital-based survey to evaluate glycemic control and complica-

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Abbreviations: DKA, diabetic ketoacidosis.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

tions of type 1 diabetes in children and adolescents.

RESEARCH DESIGN AND METHODS

— This cross-sectional survey was performed at Muhimbili National Hospital clinic for diabetes between June 2005 and February 2006 and included children aged between 5 and 18 years who had the diagnosis of type 1 diabetes for at least 6 months. A total of 99 (57 female and 42 male) of 104 children were studied.

Ethical approval was obtained from the Research and Publication Committee of Muhimbili University College of Health Sciences. Parents or guardians and children aged >12 years gave their informed consent.

A structured questionnaire was used to collect demographic data from patients and parents or guardians. The variables included were age, sex, education, occupation, frequency of complications, insulin availability, accessibility, dosage and cost, and clinic visits, as well as the possibility of blood glucose monitoring.

Each participant was questioned on the education of both the child and parents or guardians. Children reported whether they were currently going to school, and, if not, why, especially if their not going was because of type 1 diabetes. The occupation of parents or guardians was asked in addition to any sick leaves they had taken because of their child's sickness. The age at diagnosis of diabetes and the presence of DKA at the time of diagnosis were recorded.

The frequency of DKA and hypoglycemia over the last 6 months were recorded. In particular, DKA was defined as the presence of ketones in the urine, a history of an altered level of consciousness of the patient or coma at the time of assessment, or an admission to hospital over the last 6 months. Hypoglycemia was defined as the presence of three or more episodes of the following symptoms: sweating, hunger, tingling around the mouth, tremor, anxiety, weakness, headache, visual disturbances, slurred speech, vertigo and dizziness, difficulty in thinking, tiredness, drowsiness, change in affect (e.g., depressed, angry, or argumentative), mental confusion, coma, and convulsion, with these symptoms being relieved by giving the child sugar-containing foods.

Insulin availability and accessibility were assessed. Furthermore, the dosage of insulin and cost of insulin per vial were recorded. The possibility of getting insulin at a reduced cost or free was questioned as well as any assistance from relatives, employer, diabetes clinic, or nongovernmental organization. We grouped children who missed insulin doses over the last 6 months into those who never missed a dose, those who missed five times in a month, those who missed 3 days in a week, and those who missed ≥3 consecutive days. In addition, we recorded the reasons for missing the insulin dose. Finally, we asked about the possibility of measuring blood or urine glucose at home.

There were no verifications with medical records, because most of the patients did not have past medical records. Physical measurements were made by a specially trained nurse.

Anthropometric measurements

Anthropometric measurements included body weight (rounded to the nearest 100 g) and height (rounded to the nearest 0.1 cm), which were taken with subjects wearing light-weight clothes without shoes. BMI was calculated according to the Quetelet equation (weight in kilograms divided by the square of height in meters).

Laboratory procedures

Two milliliters of venous blood was taken from the anterior cubital fossa of each child, using a sterile disposable syringe and needle after a thorough cleaning of the venipuncture site with a swab soaked in 70% alcohol. One drop of blood was immediately put on the glucostick for determination of random/fasting blood glucose. The determination of blood glucose was done with a glucometer (LifeScan, Milpitas, CA). The remaining blood was put into an EDTA bottle for A1C determination. A1C was determined using a DCA2000 Hemoglobin A1c reagent kit (Bayer Diagnostics, Mulgrave, Australia).

Urine examination for microalbuminuria

Two milliliters of spot fresh urine was collected in an empty clean bottle. The urine was then examined by multisticks (Medi-Test Combi 10 SGL) to determine the presence of proteins, ketones, and sugar.

The test strip was dipped into the bottle of fresh urine for 30–60 s, and the color on the test strip was then compared with the color scale on the bottle. The minimum sensitivity of the test strip was 10 mg/dl of protein in urine. Any urine samples that were negative for proteinuria using the sticks were retested by MICROTEX (Tulip Diagnostic, Goa, India) for microalbuminuria (an indirect latex slide test for detection of microalbuminuria). One drop of clear urine was put on the glass slide using a disposable pipette, and then one drop of antihuman albumin was added on the drop of urine on the slide. The antihuman albumin reagent and urine were mixed for 30 s. One drop of well-mixed albumin latex reagent was added, and the solution was mixed uniformly over a circle. Agglutination was then observed for 3 min while the slide was rocked back and forth. Agglutination meant a negative result; no agglutination meant positive results, indicating the presence of albumin in urine (concentration >2.5 mg/dl).

Retinal examination

Fundus ophthalmoscopy was performed by the same ophthalmologist, who was dedicated to patients with diabetes. One drop of atropine was put in each eye and left for 10–30 min for the pupil to dilate. Funduscopy was then performed to examine the optic disc, macula, and retinal vessels. Retinopathy was considered when there were diabetic retinal changes.

Statistical analysis

All values are expressed as means ± SD. The overall prevalence of common complications was calculated using frequency distributions. Differences in sex variables and dichotomy variables were analyzed by Fisher's exact test. The participants were divided into three age-groups (i.e., 5–11.5, 11.5–15.5, and 15.5–18 years). Given the non–normal distribution of the variables, differences between the three groups were tested by Kruskal-Wallis testing. The statistical significance level was $P < 0.05$. Differences between groups of interest were tested by Mann-Whitney testing, adjusting the level of significance by $P < 0.0167$. All calculations were performed with the computer program SPSS (version 10).

RESULTS

— Baseline clinical characteristics, anthropometric measurements, and A1C levels are reported in Table 1. The female-to-male ratio was 1.3:1, mean ± SD age was 12.6 ± 3.5 years, duration of diabetes was 4.76 ± 3.58 years, and A1C was 10.65 ± 2.09%. Of the children, 75% presented with DKA at the time of diagnosis.

Children were grouped into prepubertal (5–11.5 years), pubertal (11.5–

Table 1—*Subjects characteristics*

	Groups				Significant differences ($P \leq 0.05$)
	All	Prepubertal	Pubertal	Postpubertal	
Age (years)	12.6 ± 3.5	8.18 ± 1.85	13.45 ± 1.25	16.13 ± 0.72	<0.001
Sex (male/female)	42/57	10/21	16/19	16/17	0.378
Height (m)	136.15 ± 21.38	123.94 ± 23.68	139.43 ± 18.01	141.46 ± 27.79	0.001
Height SDS	−2.52 ± 2.69	−2.25 ± 3.23	−3.4 ± 2.44	−2.53 ± 1.66	0.026
Weight (kg)	38.19 ± 11.32	32.10 ± 12.95	39.00 ± 9.33	49.57 ± 2.39	<0.001
BMI (kg/m^2)	20.04 ± 2.15	19.55 ± 2.0	19.92 ± 2.51	20.79 ± 2.39	0.121
BMI SDS	0.82 ± 1.38	2.11 ± 1.51	0.34 ± 0.84	0.60 ± 2.86	<0.001
A1C					
<7.5%	1 (1)	0 (0)	0 (0)	1 (13.0)	NA
7.5–10%	60 (60)	22 (68.8)	23 (67.6)	15 (45.5)	0.648
10–12.5%	14 (14.1)	5 (15.6)	5 (14.7)	4 (12.1)	0.522
>12%	24 (24.2)	5 (15.6)	6 (17.6)	13 (39.4)	0.756
Duration of diabetes					
<1 year	10 (10.1)	4 (12.2)	4 (11.8)	2 (6.1)	0.780
1–5 years	51 (51.1)	20 (62.5)	13 (38.2)	18 (54.5)	0.540
>5 years	38 (38.4)	8 (25.0)	17 (50.0)	13 (39.4)	0.126
DKA	89 (89.9)	28 (90.3)	33 (94.3)	28 (84.4)	0.437
Hypoglycemia	55 (55.6)	21 (9.7)	20 (57.1)	14 (42.2)	0.125
Retinopathy	22 (22.2)	8 (25.8)	3 (8.6)	11 (33.3)	0.043
Microalbuminuria	29 (29.3)	9 (29.9)	9 (25.7)	11 (33.3)	0.790
Insulin dosage					
0.5–0.8 units/kg	39 (39.4)	16 (50.0)	8 (23.5)	15 (45.5)	0.002
0.8–1.2 units/kg	29 (29.3)	9 (28.1)	15 (44.1)	5 (15.2)	0.669
>1.2 units/kg	31 (31.3)	7 (21.9)	11 (32.4)	13 (39.4)	0.228
Insulin available					
Yes	57 (57.5)	18 (56.3)	24 (70.6)	15 (45.5)	0.1
No	42 (42.4)	14 (43.8)	10 (29.4)	18 (54.5)	0.1
Clinic visits in last 6 months					
Months 1–3	33 (33.3)	11 (33.3)	9 (27.3)	13 (39.4)	0.253
Months 4–6	37 (35.4)	10 (27.0)	13 (35.1)	14 (37.8)	0.994
Months >6	29 (29.0)	11 (37.9)	12 (41.4)	6 (20.7)	0.763

Data are means ± SD or *n* (%). NA, not applicable; SDS, SD score.

15.5 years), and postpubertal (15.5–18 years) groups. We chose these groups because children in Tanzania start puberty at the age of 11.5 years, and they are in puberty up to age 15.5 years.

All children had poor glycemic control, except one who had good control (A1C <7.5%). A high percentage of children (24.2%) had very poor glycemic control (A1C >12.5%). However, there was no statistical difference between the A1C in all three groups ($P = 0.815$ for moderate A1C, $P = 0.141$ for poor A1C, and $P = 0.394$ for very poor A1C). The mean duration of diabetes was similar in all three groups.

The height SD score was low in all three age-groups (−2.52 ± 2.69) with even lower rates in the pubertal group (−3.4 ± 2.44; $P = 0.026$).

The overall prevalence of both acute and chronic complications was high: DKA (89.9%), hypoglycemia (55.6%), retinopathy (22.2%), and microalbuminuria (29.3%). As expected, no differences were found in acute complications (DKA and hypoglycemia) in all three age-groups.

Surprisingly, there was already a high frequency of retinopathy in the prepubertal group (25.8%). The pubertal group had a lower occurrence of retinopathy (8.6%), compared with other groups ($P = 0.043$). No significant differences were found among the three groups for microalbuminuria.

All children were receiving a conventional insulin regimen (0.5–2 units · kg^{-1} · day^{-1}). None of the children had glucose monitoring at home. Table 2 shows the frequency of children missing their insulin doses. There was no difference between the age-groups ($P = 0.172$, $P = 0.410$, and $P = 0.837$, respectively); however, there was a significant difference between those who missed insulin doses and chronic complications (retinopathy and microalbuminuria) ($P = 0.004$ and $P = 0.040$, respectively). No association was found between the number of insulin doses missed and the occurrence of acute complications (DKA and hypoglycemia; $P = 0.335$ and $P = 0.834$, respectively).

Numbers of clinic visits were similar in all the groups, with 35.4% of the children visiting the clinic four to six times in 6 months. No association was found between clinic visits and complications (data not shown).

Neither parents' or guardians' education nor occupation was associated with complications and glycemic control. There were no differences in child's education level, parents' or guardians' education and occupation, marital status, parents' or guardians' sick leaves, and insulin availability or accessibility (data not shown). There was no relationship between prevalence of complications and duration of diabetes.

Table 2—*Missed insulin by age, sex, glycemic control, and complications*

	Groups				Significant differences ($P \leq 0.05$)
	Never missed insulin	Missed insulin 5 times/month	Missed insulin 3 times/week	Missed insulin ≥3 consecutive days	
Age					
5–11.5 years	13 (35.1)	6 (42.9)	4 (21.1)	8 (27.6)	0.172
11.5–15.5 years	14 (37.8)	5 (35.7)	6 (34.5)	10 (35.4)	0.410
15.5–18 years	10 (27.0)	3 (21.4)	9 (47.4)	11 (37.9)	0.837
Sex (male/female)	16 (43.2)/21 (56.8)	6 (42.9)/8 (57.1)	7 (36.8)/12 (63.2)	13 (44.8)/16 (55.2)	0.956
A1C					
<7.5%	1 (2.8)	0 (0)	0 (0)	0 (0)	NA
7.5–10%	25 (69.4)	10 (71.4)	9 (47.4)	16 (53.3)	0.181
10–12.5%	5 (13.9)	2 (14.3)	1 (5.2)	6 (20.0)	0.804
>12%	5 (13.9)	2 (14.3)	9 (47.4)	8 (26.7)	0.271
DKA	31 (83.3)	14 (100)	17 (89.5)	27 (93.1)	0.335
Hypoglycemia	19 (51.4)	9 (64.3)	10 (52.6)	2 (6.9)	0.834
Retinopathy	4 (10.8)	0 (0)	8 (42.1)	10 (34.5)	0.004
Microalbuminuria	8 (21.6)	1 (7.1)	9 (47.4)	11 (29.3)	0.045

Data are *n* (%). NA, not applicable.

CONCLUSIONS — This is one of the few studies on complications of type 1 diabetes in children and adolescents from sub-Saharan Africa. In this survey, we documented a high prevalence of complications and poor glycemic control, reflecting a complex unfavorable social and economic environment, in which children with type 1 diabetes in Africa are living.

On the basis of recommendations from the Diabetes Control and Complications Trial, in developed countries a high proportion of children and adolescents with type 1 diabetes receive intensive treatment (14). In contrast, children in Tanzania received conventional insulin treatment regimen only irregularly. This resulted in a higher mean A1C (i.e., 12.6 ± 3.5%) than those reported in studies performed in the developed world (14,15). However, our findings were similar to those of a study done in Sudan, where Elamin et al. (16) found a high incidence of poor glycemic control estimated by A1C. Most likely the underlying cause is the association between limited insulin supply and lack of self-monitoring of blood glucose. Furthermore, in addition to limited insulin supply, patients reduce their insulin dose to ensure longer periods of insulin treatment. Nevertheless, insulin storage might also influence the effect of the insulin, as many families store the insulin in a pot with cold water, exposing the insulin to high temperatures. Correlations reported in other studies between A1C and age (14,17), number of physician visits (18,19), and duration of diabetes (14) were not found in this study, probably because of the small sample size and overall very poor glycemic control.

It was not possible to assess the correlation between A1C and frequency of self-monitoring of blood glucose (18,20–23) because none of the children had glucometers or glucosticks to perform daily blood glucose measurements. More importantly, even in hospitals, blood glucose measurements cannot be routinely performed because of the lack of facilities. In agreement with different studies (22) and different cultural backgrounds, pubertal girls presented higher mean A1C values than boys. It has been shown that linear growth might also be impaired in children even when reasonable glycemic control had been achieved (23,24), and this growth pattern is likely to be more pronounced in a setting in which metabolic control is very poor. In fact, most of our children had short stature, which was more pronounced in puberty, in accordance with other studies (25,26). At variance (27,28), there was no correlation between growth and duration of diabetes or insulin requirement (18,21); however, we cannot rule out the contribution of other well-known factors such as malnutrition and chronic infections.

The high prevalence of DKA observed in this survey (89.9%), although comparable to the prevalence found in Congo Brazzaville (10), might have been overestimated because of the arbitrary definition of DKA, leading to a higher prevalence than that reported in the international literature (25–30%) (28). Our data reflect the estimated prevalence of DKA at diagnosis (29), but we observed a much higher occurrence of DKA in children already receiving insulin supplementation. This high frequency of DKA during therapy is not likely to be affected by the arbitrary definition but more likely reflects limited insulin supply and lack of self-monitoring. In fact, lack of insulin and recurrent infections are the main reported precipitating factors for DKA in sub-Saharan Africa (30). The high percentage of symptomatic hypoglycemic episodes found in our study reflects again the poor level of glycemic control and the lack of self-monitoring. However, the true prevalence of hypoglycemia remains unknown in our study population, and the percentage might again be exaggerated as our study depended solely on self-reporting or parental reporting of these episodes in the absence of self-monitoring of blood glucose. Some studies reported that patients with type 1 diabetes who have chronically poor blood glucose control perceive hypoglycemia at higher levels than those with acceptable blood glucose control (31), suggesting the possibility that the children in our survey might have had normal blood glucose levels when they had symptoms of hypoglycemia.

Along with the high prevalence of acute complications, we documented a high prevalence of background retinopathy. Our data are similarly to those of a study done in Kilimanjaro, Tanzania, by Neuhann et al. (13), who found a prevalence of retinopathy of 14% in the whole type 1 diabetic population. Surprisingly,

in our study we detected a higher prevalence of retinopathy in prepubertal children compared with the pubertal group. This age distribution of retinopathy is alarming as it presents the possibility that some adolescents might have died because of diabetes complications. Although no studies on mortality in children and adolescent with diabetes in Africa are available, this conclusion is likely, and our results also underline the importance of metabolic control before puberty as young children are able to be affected by retinopathy. This finding is in contrast with some longitudinal studies in which the duration of prepubertal diabetes seemed to have limited effect on long-term complications (32).

This study also demonstrated a high prevalence of microalbuminuria, which was higher in the older children, in accordance with other studies (33). There was no correlation between duration of diabetes and occurrence of microalbuminuria. It is worthwhile to acknowledge that the prevalence of microalbuminuria might have been overestimated because of the methodological limitations.

In many sub-Saharan African countries, the insulin supply is erratic, and the monthly cost of insulin for an average treated patient equals 25% of the minimum wage (13). In our survey, 63.3% of children missed insulin doses at least once over the preceding 6 months mainly because of lack of funds and insulin availability. These difficulties are exacerbated by intermittent availability of supplies such as syringes, urine and blood testing strips, and, perhaps most crucially, by limited experience in the management of diabetes of most health care workers (35).

In summary, these data clearly demonstrate that insulin scarcity, poverty, and lack of adequate health care increase the incidence of complications from acute and chronic diabetes in children and adolescents with type 1 diabetes in Tanzania, a problem that previously has not been fully recognized. This survey further highlights the difficulties of getting good metabolic control, implying that major efforts are needed to improve quality of care in children with type 1 diabetes in sub-Saharan African countries. The first step is obviously to make insulin available for all children all the time.

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