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Incidence, prevalence and clinical manifestations at onset of juvenile diabetes in Tanzania

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ABSTRACT

Better knowledge on incidence, prevalence and clinical manifestations is needed for planning diabetes care in Sub Saharan Africa.

Aims: To find a crude incidence/prevalence of diabetes in children and young adults in a low resource setting, classify the diabetes and audit the health record keeping.

Methods: A retrospective observational study based on medical recordings 2010–2016. Target population was children and adolescent registered in Changing Diabetes in Children (CDiC) or Life for a Child (LFAC) programs for children with T1DM and diagnosed at 5 diabetes clinics in three geographical regions of Tanzania. 604 patients' files were available from five hospitals.

Results: 336/604 files covered patients <15 years of age at diagnosis. The prevalence of diabetes <15 years of age ranged from 10.1 to 11.9 per 100,000 children and the annual incidence 1.8–1.9/100,000 children, with peak incidence at 10–14 years. A lot of data were missing. The great majority of the patients presented with typical signs and symptoms of T1D, 83.7% with plausible ketoacidosis (DKA).

Conclusions: Diabetes incidence and prevalence is still low. T1D seems to dominate with very high frequency of DKA at diagnosis. Increased awareness of diabetes both in health care and community is needed.

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder with hyperglycaemia as the main clinical feature [1]. There are different forms of diabetes including Type 1 diabetes (T1D), Type 2 Diabetes (T2D), Malnutrition Related Diabetes, Gestation Diabetes Mellitus and other specific forms. They all differ in aetiology and pathogenesis [1–3].

Initial classification of DM is usually based on the clinical presentation and family history, but there are also other ways of classifying diabetes, using genetics and autoimmunity. In Tanzania, children with diabetes are mostly treated with

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insulin as T1D unless they have obvious signs of T2D like obesity and/or acanthosis nigricans. T1D has an abrupt clinical onset with polyuria, polydipsia and weight loss [4], with majority of patients in the western world (80–90%) having no family history of diabetes [2,4]. T1D is regarded an autoimmune disease with autoantibodies present in 85–90% of T1D cases [5]. However there are documented reports of idiopathic T1D commonly seen in African-American populations [6] in which there is lack of autoimmunity, and T1D may very well include subtypes, so far not classified. The genetic susceptibility for T1D in African people has been associated with HLA-DR3/DR4, similar to that seen in European populations [7]. T1D accounts for approximately 10% of all diabetes cases worldwide [8]. The annual incidence of T1D worldwide is estimated to be approximately 86,000 children under 15 years [9] with highest incidence in Scandinavia (Finland; 62,5, Sweden; 48,8 (14), Norway; 32,7 per 100,000) [10–12]. In Sub-Saharan Africa (SSA) incidence data are limited to single countries or do not exist. The annual incidence rate of T1D in Ethiopia (0–14 years) was estimated to be 0.3 per 100,000 in 2013 [9]. A study on juvenile DM in Dar es Salaam, Tanzania, from 1993 estimated the annual incidence to be 1.5/100,000 [13]. IDF's estimation of T1D incidence in children aged 0–14 years in Tanzania was 0.9/100,000 per year in 2013 [9]. From Zanzibar, an island in Tanzania with a mixture of Africans and Arabs, an annual incidence of T1D (0–14 years) of 2.45/100,000 has been reported [14]. Sudan had a much higher annual incidence rate of 10.3/100,000 [15]. T2D is seen primarily in adults, but with increasing obesity the trend is shifting to children and adolescents in some areas of the world [16]. Family history is very common in T2D, ranging from 74 to 100% [17].

Knowing type of diabetes and how it presents is vital in diagnosing, and managing the disease correctly. Children with diabetes in Tanzania, if at all classified, are so far classified based on history and clinical presentation. No studies have previously been done to classify paediatric diabetes in Tanzania. Therefore we aimed at looking at the presentation, prevalence and incidence of diabetes in children in Tanzania. Ethical approval was obtained from the Institution Review Board of Muhimbili National Hospital.

2. Methods

This is a retrospective observational study performed in five hospitals with diabetes services for children with diabetes in Tanzania. These were Muhimbili National Hospital (Dar es Salaam), Sekou Toure Regional Hospital (Mwanza), Kilimanjaro Christian Medical Centre (Moshi), Temeke District Hospital (Dar es Salaam) and Mnazi Moja Hospital (Zanzibar). The study took place between Jan 2017-June 2017, and included all the files of diabetic patients who were attending these clinics, and had been diagnosed with diabetes between January 2010–April 2016. A total of 604 files of children, adolescents and young adults in the five zonal pediatric diabetes clinics were screened. Out of these only 521(86.3%) had documentation of the age at diagnosis. Out of the 521, 336 were diagnosed with diabetes at the age less than 15 years, a cut-off we chose to be able to compare incidence and prevalence figures with reports from other countries. Only 320 files could used after the due screening process with complete clinical notes and data sets as per the protocol.

A case record form (CRF) was used to collect data from the files. The variables included demographic factors, age at diagnosis, duration of diabetes and clinical presentation. Clinical presentation at onset included: supposed diabetic ketoacidosis (sDKA) (either measured pH < 7.30 and/or nausea and vomiting, lethargy or drowsiness), polyuria, polydipsia and weight loss, as well as height and weight and blood pressure, and laboratory values of blood glucose and HbA1c.

2.1. Statistical analysis

Statistical analysis was performed using SPSS version 24.0 and excel version 14.1.0. Continuous variables were presented as means ± SD and medians and interquartile range (IQR), whereas categorical variables were presented as frequencies and percentages. Differences in dichotomous variables were analysed using Chi-square test. The difference was statistically significant if p value was <0.05.

3. Results

3.1. Characteristics of patients

The overall sex distribution among the 604 patients was similar among females (52%) and males (48%). The average age at diagnosis, among the 521 with that information, was 13.4 ± 5 years (median: 14.0 and IQR: 11.0–17.0) with mean age ranging from 11.9 ± 5.4 years in Muhimbili National Hospital (MNH) to 16.2 ± 4.9 years in Temeke.

Regarding the 320 patients with useful information found, all had normal blood pressure (106 ± 12/66 ± 9.). Only 10 out of 320 patients (3.1%) from all five hospitals had recordings of weight and height at diagnosis. Furthermore, only 160 (30.6%) patients had recordings of family history of diabetes. Having a first degree relative with diabetes ranged from 9.5% in Kilimanjaro Christian Medical Centre (KCMC) to 45.3% in Temeke hospital Table 1.

3.2. Prevalence and incidence rates

Prevalence and incidence rates of T1D in children (<15 years) were estimated for the following regions; Dar es Salaam, Kilimanjaro and Zanzibar. Table 2 shows prevalence and annual incidence for each respective region.

Prevalence rates are presented per 100,000 children, whereas incidences are estimated per 100,000 person-years (PYs). The prevalence was estimated to be 10.7/100,000 children in Dar es Salaam Region (MNH, Temeke), 11.9/100,000 in Kilimanjaro Region (KCMC) and 10.1/100,000 in the Zanzibar island. Annual incidence rate was estimated to be 1.8 new cases per 100,000 children in both Dar es Salaam and Kilimanjaro, and 1.9 new cases per 100,000 in Zanzibar.

3.3. Symptoms

Symptoms at clinical onset of DM in our study population is presented in Table 3, along with the frequency of supposed DKA at diagnosis.

Table 1 – Baseline characteristics of patients at diagnosis distributed by hospital. Percentage (%) in brackets if not otherwise mentioned.

Characteristics	Total *n* (%)	Mnazi Mmoja	MNH	Sekou Toure	KCMC	Temeke
Overall	320(100)	62(19,4)	84(26,3)	43(13,4)	66(20,6)	65(20,3)
Sex						
Female	166(52,4)	38(62,3)	44(53,0)	21(50,0)	36(54,5)	27(41,5)
Male	151(47,6)	23(37,7)	39(47,0)	21(50,0)	30(45,5)	38(58,5)
Missing	3(0,9)	1(1,6)	1(1,2)	1(2,3)	0(0,0)	0(0,0)
Age (years)						
0–9	58(18,4)	9(15,3)	26(31,3)	3(7,0)	15(22,7)	5(7,7)
10–14	119(37,7)	27(45,8)	31(37,3)	17(39,5)	27(40,9)	17(26,2)
15–17	76(24,1)	14(23,7)	12(14,5)	17(39,5)	18(27,3)	15(23,1)
≥18	63(19,7)	9(15,3)	14(16,9)	6(14,0)	6(9,1)	28(43,1)
Mean (SD)	13,4(5,0)	13,2(4,3)	11,9(5,4)	14,1(3,6)	12,2(4,6)	16,2(4,9)
Median (IQR)	14,0(11,0–17,0)	13,0(11,0–16,0)	12,0(8,0–16,0)	15,0(13,0–16,0)	13,0(10,0–16,0)	16,0(13,0–20,0)
Missing	4(1,3)	3(4,8)	1(1,2)	0(0,0)	0(0,0)	0(0,0)
BMI						
Mean (SD)	18,1(3,5)	N/A*	N/A	17,0(2,5)	18,4(4,5)	N/A
Median (IQR)	18,3(15,2–20,0)	N/A	N/A	18,2(14,6–19,0)	17,9(14,4–22,8)	N/A
Missing	310(96,9)	61(98,4)	84(100,0)	38(88,4)	62(93,9)	65(100,0)
SBP (mmHg)						
Mean (SD)	106(12)	107(12)	N/A	110(11)	100(5)	102(12)
Median (IQR)	105(99–115)	105(100–120)	N/A	110(100–120)	101(96–104)	100(93–112)
DBP (mmHg)						
Mean (SD)	66(9)	65(12)	N/A	69(8)	64(3)	64(9)
Median (IQR)	65(60–70)	64(60–70)	N/A	70(62–75)	64(60–67)	60(59–70)
Missing	232(72,5)	36(58,1)	84(100,0)	20(46,5)	60(90,9)	32(49,2)
Family history of Diabetes						
Yes	49(30,6)	16(28,6)	N/A	7(23,3)	2(9,5)	24(45,3)
No	111(69,4)	40(71,4)	N/A	23(76,7)	19(90,5)	29(54,7)
Missing	160(50,0)	6(9,7)	84(100,0)	13(30,2)	45(68,2)	12(18,5)

* N/A = not available, SD = Standard deviation, IQR = Interquartile range, SBP = Systolic blood pressure, DBP = Diastolic blood pressure.

The majority of patients who had documentation of symptoms in medical records presented with typical symptoms of T1D. Weight loss was poorly documented (missing rate; 76.7–100%). However, among those who had reports about weight changes, 56.1% had experienced unwanted weight loss. In addition, 80.5% of the patients who had medical records of symptoms experienced polyuria and/or polydipsia at clinical onset of DM.

Among those who had documentations of DKA, 83.7% presented with sDKA at diagnosis ranging from 68.8% in KCMC to 94.1% in Mnazi Mmoja hospital (Table 3). sDKA remained very high even in patients coming from families with history of DM Among the participants that had family history, 91.7% presented with sDKA at diagnosis, compared to 85.7% of the patients who did not have family history. Among children (<18 years), the majority of our patients had sDKA at diagnosis. Out of patients aged 10–14 years 87.9% had sDKA at onset but less often (69.2%) in the younger age group (<10 years).

3.4. *Laboratory data*

Only 79/320 (25.2%) participants had any blood glucose, often called fasting blood glucose, recorded in medical records at diagnosis. 67/79 (84.8%) had blood glucose ≥7 mmol/L indicating DM. The 12 patients who had lower values had other criteria fitting with the diagnosis, explaining why they were not excluded. Overall mean plasma glucose was 14.2 ± 7.0 mmol/L, ranging from 8.1 ± 2.4 mmol/L in KCMC to 16.0 ± 7.1 mmol/L

Table 2 – Prevalence per 100,000 children (<15 years) and annual incidence of T1D in children (<15 years) per 100,000 person-years (PYs) in the years 2010–2015 in three regions in Tanzania.

Region	Prevalent cases (*N*)	Incident cases (*N*)	Child population (<15 years) (31)	Prevalence per 100,000	Incidence per 100,000 per year 2010–2015)
Dar es Salaam	148	149	1,379,195	10,7	1,8
Kilimanjaro	74	66	619,953	11,9	1,8
Zanzibar	56	62	554,017	10,1	1,9

*N = number.

Table 3 – Symptoms at presentation of DM and frequency of supposed DKA(sDKA) at diagnosis in our study population (n = 320) per hospital visited. Percentage (%) in brackets if not otherwise mentioned.

Symptoms	Total *n* (%)	Mnazi Moja	MNH	Sekou Toure	KCMC	Temeke
Overall	320(100)	62(19,4)	84(26,3)	43(13,4)	66(20,6)	65(20,3)
Weight loss						
Yes	23(56,1)	10(90,9)	N/A	2(20,0)	3(33,3)	8(72,7)
No	18(43,9)	1(9,1)	N/A	8(80,0)	6(66,7)	3(27,3)
Missing	279(87,2)	51(82,3)	84(100,0)	33(76,7)	57(86,4)	54(83,1)
Polyuria and/or Polydipsia						
Yes	62(80,5)	19(95,0)	N/A	9(60,0)	6(50,0)	28(93,3)
No	15(19,5)	1(5,0)	N/A	6(40,0)	6(50,0)	2(6,7)
Missing	243(75,9)	42(67,7)	84(100,0)	28(65,1)	54(81,8)	35(53,8)
sDKA						
Yes	77(83,7)	16(94,1)	N/A	18(78,3)	11(68,8)	32(88,9)
No	15(16,3)	1(5,9)	N/A	5(21,7)	5(31,3)	4(11,1)
Missing	228(71,3)	45(72,6)	84(100,0)	20(46,5)	50(75,8)	29(44,6)

*N/A = not available.

in Mnazi moja hospital. Only 69/320(22.1%) participants had HbA1c documented in medical records at diagnosis. 58/69 (84.1%) had increased HbA1c (≥6.5%) with mean HbA1c being 10.6 ± 3.4%, lowest HbA1c in Sekou Toure hospital, Mwanza and highest in Temeke hospital, Dar es Salaam (8.0 ± 3.4 and 12.0 ± 4.5% respectively), Table 4.

Both blood glucose and HbA1c was registered in 16 patients which means that any of these values were found only in 132/320 (42.2%) of the patients. As neither blood glucose nor HbA1c were registered in the majority of the medical records, we do not know how often these parameters were used for diagnosis of diabetes in addition to clinical symptoms and signs.

4. Discussion

First and foremost, it must be highlighted that a lot of documentation was missing in the medical records from all five hospitals. Even though there is lack of resources, it should be possible and self-evident to register medical history as well as symptoms and signs, to get weight and height of every patient and also at least a blood glucose value. Those of us (EM and KR) who are working clinically with diabetes in Tanzania mean that blood glucose strips can be expected to be used in the great majority, perhaps almost all, patients at diagnosis, but evidently these values are often not registered. Occurrence of DKA must also be recorded and if possible confirmed wih pH. Even without determination of HLA or autoantibodies it is important to get a reasonably reliable classification of diabetes in children and adolescents to thereafter give an adequate treatment.

Nevertheless, the registered information found in the medical records about the clinical manifestation and medical history fits with the diagnosis T1D. We cannot say whether this is the autoimmune type of T1D or so called idiopathic form of insulin dependent diabetes. Most of these patients were severely ill. The great majority of those, where we found registration, had sDKA at diagnosis, even in families with a family history of diabetes. Therefore it is of utmost importance to spread information about diabetes, to increase awareness both in the general public and among health care staff.

Table 4 – Laboratory data at diagnosis of diabetes in each respective hospital. Percentage (%) in brackets if not otherwise mentioned.

Clinical signs	Total *n* (%)	Mnazi Moja	MNH	Sekou Toure	KCMC	Temeke
Overall	320(100)	62(19,4)	84(26,3)	43(13,4)	66(20,6)	65(20,3)
Plasma glucose (mmol/L)						
≥7 mmol/L	67(84,8)					
Mean (SD)	14,2(7,0)	16,0(7,1)	N/A*	12,6(6,6)	8,1(2,8)	14,2(6,8)
Median (IQR)	14,1(8,7–18,2)	15,2(10,7–21,1)	N/A	10,3(8,9–14,9)	7,4(6,2–10,5)	14,7(8,9–16,9)
Missing	241(75,3)	29(46,8)	84(100,0)	26(60,5)	61(92,4)	41(63,1)
HbA1c %						
≥6,5%	58(84,1)					
Mean (SD)	10,6(3,4)	10,7(3,3)	N/A	8,0(3,4)	11,7(2,5)	12,0(4,5)
Median (IQR)	10,6(7,6–14,0)	10,7(7,4–14,2)	N/A	7,0(5,8–10,0)	11,4(9,9–14,6)	14,0(10,6–14,0)
Missing	251(78,4)	54(87,1)	84(100,0)	24(55,8)	30(45,5)	59(90,8)

* N/A = not available, SD = Standard deviation, IQR = Interquartile range.

Incidence and prevalence rates were estimated based on the 320 out of 604 patients with useful information who were diagnosed with DM < 15 years). Although it would be interesting to know more about patients aged 15–18 years, and newly-diagnosed young adults, we chose 15 years as cut-off to be comparable with other countries and reports regarding incidence and prevalence. All patients recruited were classified as T1D, by their clinical characteristics (polyuria, polydipsia, weight loss), and often presence of sDKA at diagnosis. Hence the estimations of incidence and prevalence are for T1D. The annual incidence was between 1.8 and 1.9/100,000 children in the three zones we included, which is slightly higher than found in a previous study [13]. However, still underestimation is plausible because of many missing data for those recorded, and probably because of missed diagnosis. We have no possibility to know how many children could have died in DKA without being diagnosed as diabetes. Anyhow, our data are comparable to another study which estimated up to 75% missing diagnosis [9]. In our study prevalence ranged from 10.1 to 11.9 cases per 100,000 children in three different geographical regions in Tanzania, calculated based on last census [18]. The annual population growth is estimated at a rate of 2.5% per year [19] However, our estimates were based on diagnosed cases from medical records rather than population screening which means that children with undiagnosed diabetes cannot be estimated. According to a previous study 75% undiagnosed diabetes in Tanzania, including children, died before diagnosis [20]. Zanzibar has a mixed ethnic population with Arabs from the Sultanate of Oman. The annual incidence of T1D in the Sultanate of Oman (18) was higher than the estimated incidence in Zanzibar. While Zanzibar's incidence was closer to incidence rates in other regions in Tanzania (Table 1). This supports the interpretation that geographical variation in incidence of T1D in Africa may partly be explained by different levels of disease awareness.

The mean age at diagnosis for the total cohort (604 patients) was 13.4 ± 5.0 (Median: 14.0 IQR: 11.0–17.0) with a peak incidence in the age group 10–14 years, which is similar to what is been reported elsewhere [14]. One reason to the very low incidence in children 0–9 years in Tanzania may be that many younger Tanzanian children are never diagnosed but die before diagnosis. This is supported by the lower incidence of sDKA at diagnosis in the young age group, in contrast to other studies, which may be attributed to too late diagnosis of diabetes with high mortality.

In this study there is no difference in female:male ratio, 1.1:1, observed in other African countries [14]. However Zanzibar, whose population partly has Arab ethnicity, had more female patients (62.3% female vs 37.7% male) which is in accordance to other Arab Countries [21] which differs from what is seen in several caucasian populations where T1D is slightly more common among boys <15 years of age and >15 years of age twice as common among males as among females. Of the children with documentation regarding family history of diabetes, 30.6% had first degree relatives which is 2–3 times more common than generally observed in western countries [1,2]. An explanation may be that the young patients with family history survive more often than those with no family history, because of greater awareness of the disease in families where somebody already has DM.

Supposed, although not always validated. DKA (sDKA) at presentation was up to 83.7%. This is more common than the previous study done in one centre in Tanzania which found 75% (19). Similar percentages have been reported in other developing countries [14,22]. Surprisingly, having a relative with diabetes did not reduce the risk of sDKA at diagnosis. As has been found in other studies [23]. Probably poor socioeconomic situation, may explain the lack of association. Out of those who had documentation of symptoms in medical records, most had typical symptoms of polyuria, polydipsia and weight loss, yet the majority were not diagnosed until sDKA developed. It is apparent that more education is needed on T1D to get earlier diagnosis and prevent DKA. The effect of educational campaigns to improve awareness has been demonstrated in a community in Italy where the frequency of DKA at diagnosis was reduced from 78% to 12.5% [24].

5. Conclusions

The incidence of diabetes <15 years of age in Tanzania ranges between 1.8 and 1.9/100,000 children, year with a peak of the diagnosed cases at the age of 10–14 years, which most probably is an underestimation, while the prevalence ranged from 10.1 to 11.9 cases per 100,000 children. Most of the patients have symptoms and signs suggesting T1D.

There seems to be a very high rate of DKA at diagnosis and most probably many patients, especially young children, are never diagnosed but die. Unfortunately a lot of data are missing from medical records, which limits the conclusions. Even though there is lack of resources, it should be possible and self-evident to register medical history as well as symptoms and signs, to get weight and height of every patient and also at least a blood glucose value. Occurrence of DKA must also be recorded.

There is considerable scope to decrease morbidity and mortality of diabetes through diabetes education and awareness programs.

5.1. *Recommendations*

Increase efforts to enhance public and medical awareness of the presenting features of T1D in the young population. Improving records keeping may lead to improved patient care and better delineation of the paediatric diabetes burden in Tanzania.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107817.

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