Keto-acidosis at diagnosis of type 1 diabetes in children and adolescents in Lagos, South-West Nigeria: the pattern over 10 years

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Abstract

Diabetic ketoacidosis (DKA) is the most serious complication in newly diagnosed cases of type 1 diabetes. We have determined the frequency of DKA at diagnosis in children with type 1 diabetes in Lagos University Teaching Hospital over a 10-year period, and have compared rates for the earlier and later years of the study period. This was a retrospective review of the case records of all the patients diagnosed with type 1 diabetes over a 10-year period from 2005 to 2015. Fifty-six (56) patients (26 males; 30 females), were seen with a mean age at diagnosis of 9.7±3.9 years. Thirty-one (31) patients (55%) presented with DKA at diagnosis. The mean age at diagnosis of the patients with DKA (8.7±3.4) was lower that of the patients without DKA (11.0±4.0, p=0.021). The median duration of symptoms before presentation in the DKA group was lower than the non-DKA group (three vs four weeks, p=0.002). Patients aged 5.0–10.9 years constituted more than half (58%) of the patients presenting with DKA. The younger age group has a greater tendency to present with DKA (p=0.004). The rate of DKA was higher in the Yoruba than the Ibo ethnic groups (p=0.007). The frequency of DKA at diagnosis in the latter years (47.4%) reduced by a quarter from the rate of 72% in the earlier years (p=0.076). We conclude that the rate of DKA at diagnosis is still unacceptably high, although has shown a slight reduction in more recent years.

Introduction

Type 1 diabetes is increasing in incidence worldwide at a rate of 2–5% per year, and approximately 200 children are diagnosed with new-onset type 1 diabetes every day.[1]

The clinical presentation of type 1 diabetes can be acute or insidious. It is generally easy to diagnose based on a history of polyuria, polydipsia, polyphagia, weight loss, and generalised body weakness, together with simple bedside tests such as urine dipsticks and glucose test strips.[2] Diabetic ketoacidosis (DKA) is the most serious complication in newly diagnosed cases of type 1 diabetes and also the leading cause of death in these children.[3] Early insulin replacement prevents DKA, thus the presence and severity of DKA is largely a consequence of delay in diagnosis and initiation of insulin therapy.[4]

There is wide geographic variation in the frequency of DKA at onset of diabetes.[5,6] This ranges from 13 to 70% in Europe and North America and up to 80% in the United Arab Emirates.[5,6] African studies have documented rates of DKA at initial diagnosis in type 1 diabetes as low as 33%,[7,8] while the majority of other centres reported higher rates approaching as high as 88%.[9–16]

Diabetic ketoacidosis is associated with significant morbidity and mortality in the paediatric population.[5,17,18] Cerebral injury is the major cause of morbidity and mortality in children and cerebral oedema accounts for 60–90% of all deaths from DKA.[5,17,18] Other complications include hypercoagulability leading to stroke and deep vein thrombosis, rhabdomyolysis, pulmonary and gastrointestinal complications, and long-term memory dysfunction.[5,18]

The subspecialty of paediatric endocrinology is developing in Nigeria with the creation of the African Paediatric Endocrinology Training Centres, first in Nairobi, Kenya (2008) and later Lagos, Nigeria (2012), resulting in the creation of an awareness of the importance of early detection of symptoms of paediatric endocrine disease, especially diabetes. Hence, this study sought to determine the frequency of DKA at diagnosis in children presenting with type 1 diabetes in Lagos University Teaching Hospital over a 10-year period, and also to compare the frequency of DKA at diagnosis between the earlier five-year period (before the effective development of the subspecialty of paediatric endocrinology) and the latter five-year period. The aim was to

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	All patients (n=56)	DKA (n=31)	Non- DKA (n=25)	Significance
Male Female	26 (46%) 30 (54%)	16 15	10 15	p=0.386
Socioeconomic status High Middle Low	 9 (16%) 24 (43%) 23 (41%)	 5 16 10	 4 8 13	p=0.279
Age at presentation (years) Mean±SD Median	 9.7±3.9 10	 8.7±3.4 9	 11.0±4.0 11	p=0.021*
Duration of symptoms (weeks) Mean±SD Median	 5.4±4.6 4.0	 3.4±0.9 3.0	 7.1±5.8 4.0	p=0.002*
HbA1C at presentation (%) Mean±SD Median	 12.1±1.9 12.0	 12.0±1.7 12.0	 12.2±2.1 13.5	p=0.728
*Significant (p<0.05).				

Table 1. Socio-demographic and clinical characteristics of the patients

Age group	All patients (n=56)	DKA (n=31)	Non-DKA (n=25)
0–4.9 years	9 (16%)	6 (19%)	3 (12%)
5–10.9 years	23 (41%)	18 (58%)	5 (20%)
11–14.9 years	18 (32%)	6 (19%)	12 (48%)
≥15 years	6 (1%3)	1 (4%)	5 (20%)
Total	56 (100%)	31 (100%)	25 (100%)

Table 2. Patients' age group at presentation

provide information on any possible impact of awareness programmes or the need to increase the intensity of awareness-creation programmes.

Patients and methods

This was a retrospective study in which data were extracted from the case records of all the patients diagnosed with type 1 diabetes at the Lagos University Teaching Hospital from 1 October 2005 to 30 September 2015. Socio-demographic information such as age at presentation and presenting symptoms (especially whether symptoms of DKA was present or not) were extracted. Other relevant information such as duration of symptoms before presentation, investigation results, complications, family history of diabetes, and management were also extracted. The socio-economic status of the patient was determined by modifying the Oyedeji[19] classification based on the educational attainments and occupations of parents or their substitutes. DKA was defined as 'symptoms of ketoacidosis in combination with biochemical parameters of hyperglycaemia (blood glucose >11 mmol/l), serum bicarbonate <15 mmol/l, and ketonuria', in accordance with International Society for Pediatric and Adolescent Diabetes (ISPAD) and European Society for Paediatric Endocrinology/ Lawson Wilkins Pediatric Endocrine Society Consensus guidelines.[5,17]

The Health Research and Ethics Committee of Lagos University Teaching Hospital approved the study and waived the requirement for informed consent. Data extracted were collated on a Microsoft 2010 excel sheet and analysed with SPSS version 20. Univariate analysis was carried out for all major variables of interest. Continuous variables were tested for skewness of distribution. Normally distributed variables are presented as means (±SD) while skewed data were summarised using median with minimum and maximum values (range). Chi-square analysis was used to compare differences between proportions while Student's t-test was used to compare differences between means. Fisher's exact test was used to determine statistical significance when small numbers of patients were involved in analysis. A p value of <0.05 was considered statistically significant.

Results

There were 59 registered patients with new type 1 diabetes during the study period; three had incomplete data and were withdrawn, leaving 56 patients. They comprised 26 males and 30 females (M:F ratio 1.0:1.1). Other demographic information is shown in Table 1. There was no significant difference between the DKA and non-DKA groups in terms of socioeconomic status, and gender distribution or glycated haemoglobin (HbA1c) at presentation. The DKA group, however, were younger (8.7±3.4 vs 11.0±4.0 years, p=0.021), and had a shorter duration of symptoms at presentation (3.4±0.9 vs 7.1±5.8 weeks, p=0.002).

Table 2 shows the age distribution of the group as a whole, and those presenting with and without DKA. It can be seen that the younger age group had a higher tendency to present in DKA, which was statistically significant (Fisher's exact test p=0.004).

The various ethnic distributions of the patients are shown in Figure 1. The Yoruba tribe, which is the predominant tribe in the study population constituted almost

40% of the patients followed by the Ibo tribe. The other tribes were also represented to a lesser degree as shown in the figure. In comparing DKA versus non-DKA presentation in the two major ethnic groups represented, the patients from the Yoruba tribe had a higher tendency to present in DKA (68% vs 32%) than the Ibo tribe in whom only one quarter presented in DKA (25% vs 75%). This was statistically significant (Chi-square p=0.007).

	Earlier 5 years (n=18)	Later 5 years (n=38)	Significance
Male Female	7 (39%) 11 (61%)	19 (50%) 19 (50%)	p=0.436
Age at presentation (years) (mean±SD)	10.5±4.4	9.3±3.6	p=0.278
Duration of symptoms (weeks) (mean±SD)	6.7±5.4	4.5±4.0	p=0.115
HbA1C at presentation (%)(mean±SD)	12.7±1.7	11.8±1.9	p=0.106
Mode of presentation DKA Non-DKA	 13 (72%) 5 (28%)	 18 (47%) 20 (53%)	p=0.076

Table 3. Comparison between the earlier 5-year period (1 October 2005 to 30 September 2010) and later five-year period (1 October 2010 to 30 September 2015)

Table 3 compares characteristics of patients presenting in the first five years of the study (1t October 2010 to 30 September 2010) and the second five years (1 October 2010 to 30 September 2015). There was no significant difference in gender distribution, age at presentation, duration of symptoms or HbA1c at presentation. However, there was a significant reduction in those presenting in DKA: 72% in the first five years, compared with 47% in the second five years (p=0.076).

Discussion

The prevalence of DKA at diagnosis in the children with diabetes observed in the index study was 55%. This is lower than rates of between 62 and 82% reported in other studies from different regions of the country (such as Port Harcourt, Sokoto, Abakiliki, Jos, and Benin) 9–13 and other parts of Africa.[15,16] However, this rate was also lower than those reported from some Nigerian studies,[7,8] and many other countries such as Congo,[14] Kuwait,[20] Iran,[21] New Zealand,[22] USA,[23] and Finland.[24] The differing rates of DKA at diagnosis of type 1 diabetes may be associated with many factors. An inverse relationship between background incidence of diabetes and occurrence of ketoacidosis at diagnosis has been documented.[4,6] Other factors include predominant age of the study population, presence or absence of family history of diabetes, and family socioeconomic status.[4] In addition to being a reflection of a delayed diagnosis and treatment, DKA at diagnosis has also been opined as possibly signifying an aggressive form of diabetes.[25]

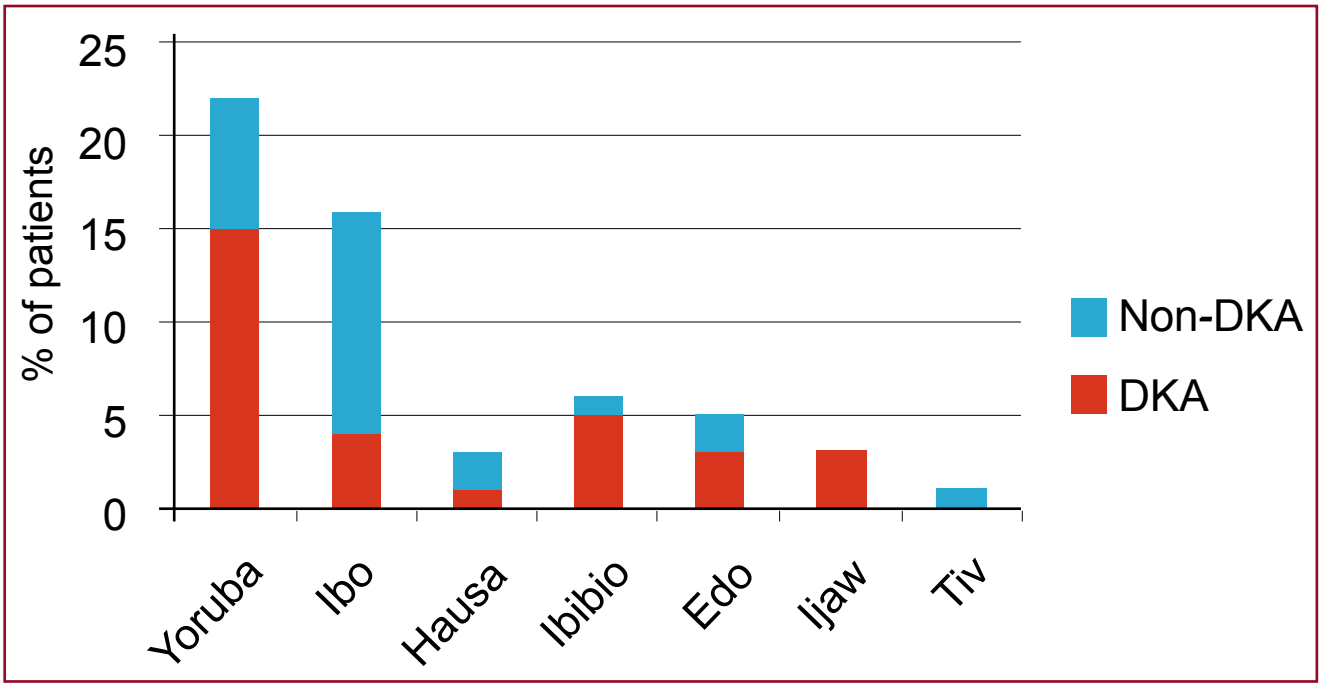

Figure 1. Ethnicity of the patients with modes of presentation (DKA versus non-DKA)

The overall mean age at diagnosis of our patients was lower than the age reported in other centres from the country, which had led some previous studies to conclude that type 1 diabetes presents at a later age in Nigeria.[7,13] While that may be a possibility, other factors such as missed diagnosis, and possibly death before diagnosis16 may be contributing to the younger age group not being picked up, patients may also not be able to express their symptoms, and also many health facilities in the country do not have the ability to routinely test for blood glucose.[26] However, the mean age in this study is slightly lower than other studies from South Africa[15] and Iran[21] respectively.

In comparing the mean age at diagnosis between the DKA and non-DKA groups, this was significantly lower in the children presenting with DKA, as has been documented by other authors.[15,21] Furthermore, it was noted that the younger age groups were more likely to present in DKA as has been noted in many other studies.[4,5,15,22] Contributing factors may include difficulty in recognising polyuria in toddlers who still wear nappies and failure of the younger age group to verbalise complaints to their care givers. However, this trend is changing for the better in some populations like Finland, as a result of intensified awareness campaigns leading to earlier diagnosis with milder metabolic decompensation in very young children.[24]

The mean duration of symptoms before presentation was significantly shorter in children who presented in DKA than those who did not. Similar findings have been reported from previous studies from Nigeria, South Africa, Iran, and Kuwait.[13,15,20,21] It has been postulated that this may be related to an aggressive and fulminant form of type 1 diabetes.[5,21,25]

With regards to ethnicity, there was a significant difference in the rates of presentation in DKA between the two tribes who are the major inhabitants in the geopolitical zone where the index study was conducted. Other studies have equally shown ethnicity to affect presentation in DKA.[22,27] Factors that may account for these findings include sociocultural issues that may in turn affect health-seeking behaviour[28] and genetic predisposition to DKA at diagnosis.[4,25] Ethnicity has also been shown to affect rates of DKA at diagnosis, even when socioeconomic status and access to health insurance were similar in the patients.[22,27]

In comparing changes over time, despite not being statistically significant, the rate of DKA in the index study reduced by one quarter in the latter five years compared with the earlier five years of the study period. This slight reduction may be due to the creation of more awareness by the availability of more trained personnel in Lagos. This is similar to the finding by a northern Finland study over a period of 20 years, comparing an earlier 10-year period (1982–1991) and a later 10-year period.[24] In contrast, in a previous Nigerian study,13 the rate of DKA at diagnosis (82% vs 73%, p>0.005) did not change significantly over an earlier eight-year period (1996–2003) and a later 8-year period (2004–2011). A lack of further significant reduction over 15 years (1999–2013) was also documented by Jeffries et al[22] in Auckland after an initial reduction over the period 1988–1996 from 68% to 42%, which suggested that factors beyond 'awareness' may be important contributors to the risk of DKA at diagnosis. Therefore, in addition to creating more awareness, future studies and strategies aimed at reducing the rate of DKA at diagnosis of type 1 diabetes should address other factors that may be contributing to children still presenting in DKA at diagnosis.

In the present study only 16% of the patients belonged to the high socioeconomic class. Even though there was no significant difference with regards to presenting with or without DKA at diagnosis, this has great implications for the care patients receive. Health insurance services are still very rudimentary in Nigeria and in many instances do not cater for chronic illnesses. Children with DKA often require prolonged hospitalisation or intensive care, imposing a great economic burden on families and health services in general.[22,29]

One limitation of this study is its retrospective nature. Future studies are needed to elucidate other factors, such as genetics, that may contribute to DKA at diagnosis in patients with type 1 diabetes. In conclusion, the rate of DKA at diagnosis of type 1 diabetes in our study is still unacceptably high, but shows a slight reduction over a period of 10 years. The younger age group is more prone to this form of presentation. It is imperative that awareness campaigns targeted at the populace on the symptoms of the disease, and also to health workers for prompt diagnosis and appropriate treatment, should be intensified to prevent DKA at presentation of type 1 diabetes and its attendant complications.

Author declaration

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Any ethical issues involving humans or animals: none.
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