Original Article

PREVALENCE AND CLINICAL CHARACTERISTICS OF NIGERIAN PATIENTS WITH EARLY-ONSET TYPE 2 DIABETES

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ABSTRACT

Background
The prevalence of early-onset type2 diabetes is increasing, and there are indications that the clinical characteristics may be different from late-onset type2 diabetes. The objective of this study was to determine the prevalence of early-onset T2D among the clinic population of a tertiary academic health centre in Nigeria and to describe and compare the clinical characteristics of early and late-onset T2D.

Method
Demographic and clinical parameters were retrospectively retrieved from the case records of patients in the clinic registry of a diabetes clinic of an academic health institution. Patients with clinical T2D diagnosed =40 years (Early Onset T2D- ET2D) were compared with T2D patients diagnosed at >40 years (Late Onset T2D- LT2D). Data were captured and analysed using SPSS version 20. Categorical variables in the two groups were compared using Chi-Square, while continuous variables were compared using Student's t-test.

Results
Out of 589 subjects with complete data, 256 (43.5%) were males and had a mean current age of 60.1 (11.6) years and median diabetes duration of 10.0 (IQR 14.7). Prevalence of subjects with early-onset diabetes in the cohort was 17%. Diabetes duration was longer in ET2D than LT2D {10 (IQR 14.8) versus 7.0 (8.0), p = 0.000}. Proportion of ET2D with poor glycaemic control was significantly higher compared to LT2D {54 (70.1) versus 204 (53.3), p = 0.007}. Also more ET2D were on insulin compared with LT2D {31 (33.0) versus 97 (20.8), p = 0.029}.

Conclusion
ET2D patients of this Nigerian population appear to be significantly different in some clinical profile from LT2D. This may imply a possible lifetime increase in microvascular complications and cardiovascular events in a productive age group of society.

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INTRODUCTION

The incidence of type 2 diabetes (T2D), the commonest form of diabetes among youth and younger adults has increased dramatically in recent times(1)(2). The increasing rate of T2D among younger adults is a departure from the typical presentation in middle age and older adults. Additionally, the incidence and prevalence of T2D in youths and young adults vary depending on the races and ethnicities with the highest occurrence among African Americans (3). Amongst native black Africans, the proportion of adults with diabetes between 20-39 years has increased to about 40%(4). The significance of this rising incidence in Africa's most productive age group has not been well investigated.

Evidence is accumulating that the course and outcome of management may be different depending on whether T2D occurs earlier or later in life (5) (6) (7) (8). Glycaemic control was worse in adults <65 years compared to adults 65 years and above(9). Earlier onset T2D impacted severity of retinopathy(10). Early-onset T2D has a lifetime risk of cardiovascular complications and this occurs at early stage of life than late-onset T2D(11)(12). Furthermore, mortality is substantially increased in patients with early-onset diabetes after the first vascular event(13). Therefore, these subjects have become a clinical priority for individualised care and aggressive measures to prevent microvascular and macrovascular complications in early stage of life.

It is not clear whether native Africans with early-onset T2D have different clinical profile compared to the late-onset subjects. In this study, we sought to determine the prevalence of early-onset T2D among the clinic population of a tertiary academic health centre in Nigeria and explore possible clinical differences between early and late-onset T2D.

Methodology

A retrospective study was carried out involving patients attending the diabetes clinic of the University College Hospital (UCH), Ibadan, Nigeria. Ethical permission was granted by the University of Ibadan and University College Hospital Joint Ethical Committee (UI/UCH Ethics Approval Number: UI/EC/18/0101). The UCH is an over 800-bedded academic tertiary health institution and a key referral centre from the southwest zone of the country. Demographic and relevant clinical variables were extracted from a clinic registry compiled between 2009 and 2010. Data were compared between all patients first

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diagnosed as T2D at the age of 40 years or below (defined as early-onset T2D) and those first diagnosed as T2D above 40 years of age (defined as late-onset T2D). Diagnosis of T2D was based on WHO 1999 criteria (14). Out of a total of 735 subjects in the database compiled then and with complete relevant data, 589 were diagnosed as T2D, 34 as type1 diabetes (T1D), 8 as gestational diabetes mellitus (GDM) and the remaining 3 were unclassified. Other subjects, apart from T2D, were excluded from further analysis. Information on current age, gender, diabetes duration, diabetes and lipid treatment, body mass index (BMI) and blood pressure were obtained from the case records. The most current fasting plasma glucose (FPG) and 2-hour postprandial (2-HPP), as well as haemoglobin A1c, were also obtained. Relatively few patients had records of haemoglobin A1c results.

Data were entered into SPSS version 20 for analysis. Demographic and selected clinical characteristics of the early onset subjects were described and compared with those of the late-onset group. Continuous variables summarized as mean (SD), or median as appropriate and categorical variables summarised as frequency (percentage) were compared between early-onset and late-onset subjects, using Student's t-test and Chi-Square test, respectively. Diabetes treatment was dichotomized into either use of oral glucose-lowering agents (OGLA) or insulin/insulin-containing regimen, and this was related to early and late-onset patients. The odd of using insulin was then determined between the two groups. The two age-onset categories were related to measures of glycaemic control using the blood glucose as well as the few available haemoglobin A1c results. Good glycaemic control was considered as both FPG <130 mg/dl and 2-HPP <180 mg/dl based on blood glucose only, and value =7% based on haemoglobin A1c. Association between glycaemic control and selected clinical parameters was determined using Chi-Square while logistic regression was performed to determine independent predictors of poor glycaemic control, the latter coded as an outcome variable of interest.

Results

Out of the 589 subjects, 256 (43.5%) were males, and 333 (56.5%) were females. There was no significant difference in gender distribution between the early and late-onset patients (Table 1). The mean (SD) current age of early-onset subjects was 46.4 (9.0) years while that of late-onset was 62.9 (10.0) years. Also, the mean age (SD) at diagnosis of both early and late-onset T2D were 34.2 (4.9) and 54.6 (9.2) respectively. A total of 100 (17.0%) had early-onset diabetes while 489 (83.0%) had late-onset diagnosis. Compared to the late-onset, early-onset subjects significantly had a longer duration of diabetes, higher plasma glucose and HbA1c and, though not statistically significant, higher BMI. There was no difference in the prevalence of early-onset subjects with BMI =25 compared to late-onset group {(85.0 (85.0) and 389 (79.6)}respectively. On the other hand, late-onset subjects significantly had higher systolic BP and the prevalence of hypertension.

Table 1: Comparing demographic & clinical characteristics of early versus late subjects

Characteristic	ET2D	LT2D	P-value
Current Age in yrs.	46.4 (9.0)	62.9 (10.0)	0.000*
Age at diagnosis in yrs.	34.2 (4.9)	54.6 (9.2)	0.000*
Sex *n (%)*: Males Females	38 (38.0) 62 (62.0)	218 (44.6) 271 (55.4)	0.226
DM Duration in years (Median/IQR)	10.0 (14.75)	7.0 (8.0)	0.000**
Hypertensive *n (%)*	43 (53.1)	316 (77.1%)	0.000*
Systolic BP *mmHg*	126.9 (21.6)	133.4 (21.6)	0.008*
Diastolic BP *mmHg*	79.2 (12.3)	78.6 (13.9)	0.703
BMI	27.3 (5.3)	26.6 (4.6)	0.339
FPG *mg/dl*	156.2 (80.9)	130.9 (56.4)	0.001*
2HPP *mg/dl*	208.0 (93.6)	190.8 (86.6)	0.128
HbA1c *%*	9.5 (1.3)	7.5 (2.3)	0.045*
On Anti-lipids n (%)	27 (34.2)	129 (31.9)	0.70

* Significant p-value using Student's t-test; **Median comparison using Mann-Whitney U. Unless otherwise stated, values are mean (SD). DM= Diabetes. ET2D- Early Onset type2 diabetes; LT2D- Late-onset type2 diabetes. FPG= Fasting Plasma Glucose; 2HPP= 2-hour postprandial

table 2 shows the distribution of subjects according to the type of hypoglycaemic agents used. The odd of patients with early-onset being on insulin or insulin-containing regimen was 1.9.

Table 2: Comparison of Proportions of Subjects Using OGLA and Insulin

Types of Anti-hyperglycemic Treatment	ET2D	LT2D		P-value
Insulin	31 (33.0)	97 (20.8)	128 (22.9)	0.029*
No insulin	63 (67.0)	369 (79.2)	432 (87.1)	
Total	94 (100)	466 (100)	560 (100)	

*Significant p-value on Pearson Chi-Square test

Based on plasma glucose, the prevalence of subjects with poor glycaemic control was significantly higher in the early onset compared with late-onset T2D {54 (70.1) versus 204 (53.3) respectively}. Similarly, based on haemoglobin A1c, all the 6 subjects with available test results in the early-onset group had poor glycaemic control compared with 35 (or 59.3%) of subjects with late-onset diagnosis (Table 3). As shown in Table 4, age of onset (less than 40 years and 40 years and above) and duration of diabetes (less than 5 years and 5 years and above) were significantly associated with glycaemic control. The risk for poor glycaemic control was higher among subjects with early-onset diabetes, and those

Table 3: Comparison of Poor Glycaemic Control Between Early and Late T2D

Measure of Glycaemic Control	ET2D	LT2D	Total	P-value
By Plasma Glucose	54 (70.1)	204 (53.3)	258 (56.1)	0.007*
By Haemoglobin A1c	6 (100)	29 (54.7)	35 (59.3)	0.089

P-value on Chi-Square test

Table 4: Association Between Clinical Characteristics and Glycaemic Control of Participants

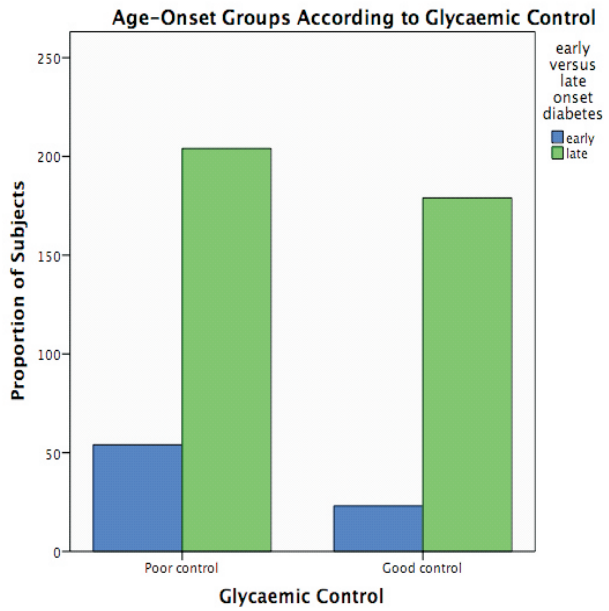
Characteristic	Poor Control	Good Control	Chi-square	P-value
Age <40 yrs.	57 (66.3%)	29 (33.7%)	4.46	0.03*
≥40 yrs.	201 (53.7%)	173 (46.3%)		
Sex Male	112 (58.6%)	79 (41.4%)	0.86	0.35
Female	146 (54.3%)	123 (45.7%)		
BMI Normal	56 (60.9%)	36 (39.1%)	1.07	0.30
Overweight /Obese	202 (54.9%)	166 (45.1%)		
Duration <5	51 (43.2%)	67 (56.8%)	10.67	0.001*
Of DM ≥5	207 (60.5%)	135 (39.5%)		
Hypertension (Systolic BP≥140 OR Diastolic BP≥90)	105 (59.3%)	72 (40.7%)	1.22	0.27
*Significant				

Table 5: Predictors of Glycaemic Control Among Participants

Predictor	Odds Ratio	Confidence Interval	P-value
Diabetes Duration			
≤ 5 years	1		0.009*
≥ 5 years	2.01	1.19 -3.46	
BMI			
Normal	1		0.205
Overweight/Obese	0.73		
Diabetes Onset			
Early	2.00	1.30 – 3.08	0.001*
Late	1		

*Significant

Figure 1



Discussion

In this study, to the best of our knowledge, we have described for the first time the characteristics of Nigerian subjects with early onset of T2D compared to those with late-onset disease and showed that the two groups were significantly different in certain clinical parameters. Prevalence of subjects with early-onset diabetes in the cohort was 100 (17%). Early-onset patients significantly had a longer duration of diabetes, had a poorer glycaemic control and were more likely to be on insulin or insulin-containing treatment regimen. There were no significant differences between the two groups in terms of cardiometabolic features such as BMI, blood pressure and use of lipid-lowering agents. Finally, age-onset of diabetes and duration of diabetes were significant independent predictors of glycaemic control in the subjects.

As inherent in most retrospective studies, there were limitations with complete data retrieval of selected variables. Also, the number of subjects with records of haemoglobin A1c results was small. This is not unusual in developing countries like Nigeria, where often there is disinclination by patients to do HbA1c, mainly because it is relatively more expensive than blood glucose. In Nigeria, health insurance coverage is very small; hence most patients pay out-of-pocket for healthcare. Furthermore, patients, many of whom are illiterate, don't appreciate the importance of HbA1c and relative superiority of the test for monitoring status of glycaemic control, even when attempts are made to explain its usefulness. Even then, our findings have shown that African patients whose onset of diabetes occurred at a younger age (= 40 years) had a different clinical profile from the typical T2D patients whose onset of disease occurred in the middle or old age.

Although data is sparse, similar studies, using different cut off age such as 30, 35 or 40 years, reported prevalence rates of early onset (or young onset) T2D ranging between 11-27.8% (15)(5)(6)(16)(7)(17). Our prevalence rate of 17% was very similar to the 18% reported in the JADE (Joint Asia Diabetes Evaluation) programme. The JADE programme(6) was a large prospective study involving 245 outpatient clinics in nine Asian countries, using 40 years age cut off for early-onset T2D participants. Our finding is however higher than 11% reported as the proportion of Nigerian T2D subjects first diagnosed between age-range 30-39 years in a cross-section of clinic population at the University of Benin Teaching hospital (18). The 30 years lowest cut off age in the Benin study could account for the relatively lower proportion of young onset diabetes

patients.

Similar to our finding, the JADE study reported median diabetes duration of 10 years (IQR 3-18 years) in the early onset subjects, which was significantly higher than the late-onset group {5 years (2-11 years)}. This is not unexpected considering the fact that those whose diabetes set in early are likely to have been in the clinic much longer than the late-onset subjects. Notably, both the current age and the age at diagnosis for both groups were significantly different.

Our study confirmed the observation by other researchers(19)(20)(21)(9) that higher proportions of early-onset diabetes subjects usually have poorer glycaemic control compared to late-onset subjects. Benhalima and colleagues (19) reported that 63% of their early-onset T2D study population still had A1c >7% after 3.2 years of follow up. This is lower than the finding of 100% in our early-onset group based on the few available HbA1c results. However, using blood glucose, the finding of 70.1% subjects with poor glycaemic control is lower is lower than 80.8% reported among Chinese population with early-onset T2D(21). Probably this is why a larger percentage of our early-onset patients were on insulin compared to the late-onset. In 7844 adults in a Health Management Office, early-onset subjects were 80% more likely to begin insulin treatment than the usual onset, with a hazard ratio of 1.8 (95% Confidence Interval 1.5-2.0), despite the similar average time of 2.2 years to requiring insulin(16). We could not retrieve sufficient information to calculate time to insulin requirement in our study sample.

The longer duration of diabetes in the early onset T2D could have significantly contributed to the poor glycaemic control and consequent earlier commencement of insulin. Among 2733 T2D British subjects, Song and co-workers(22) observed an increase in mean (SD) of HbA1c in those with diabetes duration between 10-20 years compared to <10 years duration. Additionally, T2D patients <40 years of age in each category of diabetes duration had relatively higher HbA1c. Perhaps the age onset of diabetes at diagnosis affects the state of ß Islet cells. Age at diagnosis has been shown to positively correlate with fasting C-peptide with a more rapid decline in ß-cell function in the very young patients(23).

Future prospective studies are needed to confirm our findings and to investigate their implications on the development of vascular complications in the subjects with T2D.

In conclusion, the clinical and metabolic characteristics of these Nigerian subjects with earlier onset T2D appear to be significantly different from their counterparts with late-onset. Notably, the early onset patients had a poorer glycaemic profile, which could portend a higher risk of microvascular and cardiovascular complications in the future. Interestingly, both groups had a similar distribution of cardiometabolic features.

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