

**ORIGINAL ARTICLE**

**PREVALENCE AND FAMILY HISTORY  
CHARACTERISTICS OF TYPE 1 DIABETES MELLITUS  
IN CHILDREN AND ADOLESCENTS: A NIGERIAN  
TERTIARY-HEALTHCARE BASED STUDY**

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**Abstract**

**Background:** Family history of diabetes mellitus is a useful tool for detecting children and adolescents at risk of the disease. The aim of this study is to determine the prevalence and describe the characteristics of family history of diabetes mellitus in Nigerian children and adolescents with type 1 diabetes. **Methods:** A retrospective chart review of children and adolescents newly diagnosed with type 1 diabetes was conducted in three tertiary-healthcare institutions in Nigeria. In addition to the review of charts of old patients, other children and adolescents who presented with new-onset diabetes during the review process were also included. An interviewer-administered questionnaire was used in obtaining information from the patients and their parents. Using the criteria suggested by Scheuner et al, the family history risk category was stratified into average, moderate and high. **Results:** Out of a total of 65 children and adolescents with type 1 diabetes, 29(44.6%, 95% CI= 32.6-56.7) had a positive family history of diabetes mellitus. Of the affected family members, 42.9% were first-degree relatives. The frequencies of family history risk category were average 65.5%, moderate 27.6% and high 6.9%. Among the affected family members in whom information on their diabetes status was available, 19(86.4%) had type 2 diabetes and only 3(13.6%) had type 1 diabetes. **Conclusion:** Four out of every ten patients with type 1 diabetes in the paediatric age group, have a first-degree relative with a positive family history of diabetes.

**Keywords:** Family History, Family Health History, Family Medical History, Medical Family Tree, Paediatric Type 1 Diabetes

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## **Introduction**

Family history (also referred to as family medical history or family health history or medical family tree) is a record of relevant information about medical conditions affecting a patient and his or her close family members [1,2]. It represents an essential component of a patient's medical history, typically obtained at admission to a healthcare facility as one of the components of a comprehensive patient assessment [3]. The scope of family members typically embraces three generations of relatives by birth [4] which includes the child, his/her siblings, parents, maternal and paternal grandparents and maternal and paternal aunts and uncles and first cousins [3]. Although there is no standard operational definition of a positive family history, having one or more first- or second-degree relatives who are affected with a condition is often considered a positive family history for an individual person [5]. A family history represents a valuable genomic information because it reflects the consequences of inherited genetic susceptibility, shared environmental factors and common lifestyle behaviours [6,7]. In recognition of the importance of family history, the American Society of Human Genetics states that family health history is the most important genetic test for all [8]. Although family history is easily available, inexpensive to obtain and conveniently conveys information on genes and environment shared by close relatives, it may be underutilized in health-care practice [7,9]. At the level of the individual, family history of diabetes (FHD) can serve as part of a comprehensive risk assessment required for prevention, early diagnosis and therapy of diabetes mellitus whereas at the population level, it may help tailor health-promotion messages for specific-population

groups [9].

The association between FHD and risk for the disease has been well documented with the risk varying according to which family member is affected [10,11]. Epidemiological studies have shown that the risk of developing type 1 diabetes is 8- to 15-fold higher when a first-degree relative is affected [12-15] and two-fold higher when a second-degree relative is affected [12,16]. The reports of other studies indicate that the proportion of children with affected first-degree relatives at the time of diagnosis was 10-12% [16-19]. The report of a study from the Finnish Paediatric Diabetes Register revealed that a total of 12.2% of the subjects had first-degree relatives with type 1 diabetes (father 6.2%, mother 3.2% and sibling 4.8%) and 11.9% had affected second-degree relatives [20]. Other studies have shown that 5% to 16% of children with type 1 diabetes have affected second-degree relatives with diabetes [12,13,21]. The results of a study in Oman revealed that 58.3% of children and adolescents had a positive FHD [22]. FHD has been shown to have a significant independent and graded association with the prevalence of diabetes [5,10,11]. In addition, the risk is higher when multiple family members or the father is affected, particularly if the father was below the age of 45 years at the point of diagnosis [14,23]. A family history of co-existence of both types 1 and 2 diabetes has been shown to influence the phenotype of patients with type 2 diabetes, suggesting a genetic interaction between types 1 and 2 diabetes [24]. Some studies have shown that patients with T1D have an increased prevalence of positive family history of T2D [17,18]. In Nigeria, epidemiological data on the prevalence and characteristics of FHD in children and adolescents with type 1 diabetes is scarce.

## **Subjects And Methods**

During the six-year period (January 2012 to December, 2017) covered by this review, the hospital records of all cases with paediatric diabetes mellitus admitted in the three participating Nigerian tertiary-healthcare hospitals were retrieved and audited. In addition, an interviewer-administered questionnaire was used in obtaining information from the patients and their parents. Patients with type 1 diabetes along with their parents/guardian were asked whether any biological member (i.e., blood relatives) of their family, living or deceased, had ever been told by a healthcare worker that he/she had diabetes? If the answer was yes, then the subject was asked to specify his/her relationship with the affected family member. According to the criteria suggested by Scheuner et al [25], the family history was stratified into three risk categories as follows: (i) Average: At most, one second-degree relative with diabetes; (ii) Moderate: One first-degree plus one second-degree relative with diabetes or only one first-degree relative with diabetes or at least, two second-degree relative with diabetes from the same maternal or paternal lineage; and (iii) High: At least two first-degree relatives or one first-degree plus at least, two second-degree relatives with diabetes from the same lineage [25]. In addition to the interview, the medical records of the patients were retrieved and reviewed. Ethical approval was obtained from LUTH Ethics and Research Committee. In addition, consent was obtained from the parents/guardian and when appropriate, assent from the child, respectively. Similar standards of anthropometric measurements were used in the study centres [26]. The height was measured to the nearest 0.1cm, using a stable fixed stadiometer and weight was measured to the nearest 0.1kg with the

subject in light clothing and bare foot. To minimize errors, if a duplicate measurement differed by  $> 0.5\text{cm}$  or  $> 0.5\text{kg}$  respectively, a third measurement was performed and the average of the two closest measurements was recorded as the final value. The body mass index of each of the subjects was computed, using the standard formula [26]. Using appropriate cuff, the blood pressure was measured in a sitting position after 5 minutes of rest, using a mercury sphygmomanometer. Steps were taken to ensure accuracy of all the measurements.

The data were collated and entered in Excel spread sheet. Accuracy of the data entered was double checked. Data were analysed, using Microsoft Excel and SPSS (Statistical Package for Social Sciences) version 20.0. Descriptive statistics such as frequencies, means, standard deviations were used in describing all the variables. Confidence intervals, percentages and ratios were calculated. Z-test and Student t-test were used in ascertaining the significance of difference between two proportions and means, respectively. The p-values were set at  $< 0.05$ .

## **Results**

A total of 65 children and adolescents with type 1 diabetes from three Nigerian tertiary-healthcare institutions participated in this study. The distribution of the participants according to healthcare institution was as follows: 30, 21 and 14 from University of Benin Teaching Hospital (UBTH), Benin City, Lagos University Teaching Hospital (LUTH), Lagos, and Federal Medical Centre (FMC), Gombe, respectively. There was a female preponderance with a ratio of 1: 1.75. Overall mean age at diagnosis was  $13.0 \pm 2.7$  years (95% Confidence Interval, CI = 12.3-13.7). The health-institution-

specific mean age at diagnosis were 14.3±2.4 years (95% CI =13.0- 15.6), 12.1±3.2 years (95% CI=10.7-13.5) and 11.2±3.7 years (95% CI= 10.0-12.4) in FMC, Gombe, LUTH, Lagos and UBTH, Benin City, respectively. The mean ages of patients with positive and negative family history of diabetes were 11.9±3.8 years (95% CI=10.5-13.3) versus 12.4±4.0 years (95% CI= 11.1-13.7); p < 0.05. The mean HbA1c level of all participants at admission was 10.6±2.6% (95% CI= 10.0 - 11.2). As shown in Table 1, the peak age at diagnosis was 10 to 14 years in both boys and girls. Of

the 65 children and adolescents with type 1 diabetes, 29(44.6%, 95% CI= 32.6-56.7) had a positive family history of diabetes mellitus. Healthcare institution-specific frequencies of positive family history of diabetes mellitus were as follows: FMC, Gombe 71.4% (10/14); LUTH, Lagos 42.9% (9/21); and UBTH, Benin City 33.3% (10/30). The proportion of subjects with a positive family history of diabetes mellitus was higher in Gombe (71.4%) in Northern Nigeria compared to Lagos plus Benin City (37.3%), both in Southern Nigeria, Z-statistic = 2.463, p < 0.01.

**Table 1. Age groups and gender distribution of children and adolescents with type 1 diabetes mellitus in three Nigerian tertiary-healthcare institutions**

Age groups	Males	Females	Both sexes
at diagnosis	No (%)	No (%)	Combined
Below 5 years	4(16.7)	1(2.4)	5(7.7)
5-9 years	6(25.0)	2(4.9)	8(12.3)
10-14 years	10(41.6)	21(51.2)	31(47.7)
15 years and above	4(16.7)	17(41.5)	21(32.3)
Total	24(100.0)	41(100.0)	65(100.0)

Table 2 shows that the frequency of impaired consciousness and ketoacidosis were significantly lower in subjects with positive family history of diabetes mellitus.

In addition, subjects with positive family history of diabetes mellitus had a significantly shorter mean duration of symptoms before presentation (Table 2).

**Table 2. Characteristics of subjects according to presence or absence of family history of diabetes (FHD)**

Parameters	FHD present <sup>a</sup>	FHD absent <sup>b</sup>	p-value	FHT1D present
	(n=29 subjects)	(n=36 subjects)	a vs b	(n=3 subjects)

Male (%)	34.5	38.9	> 0.05	33.3
Female (%)	65.5	62.1	> 0.05	66.7
Polyuria (%)	90.1	93.7	> 0.05	100.0
Polydipsia (%)	81.3	77.6	> 0.05	100.0
Weight loss (%)	71.0	59.2	> 0.05	66.7
Impaired consciousness (%)	38.3	63.4	< 0.05	100.0
Ketoacidosis present (%)	35.5	64.5	<0.01	100.0
Mean age at diagnosis (years)	11.9±3.8	12.4±4.0	> 0.05	10.6±3.8
Mean duration of symptoms (days)	17.8±3.6	28.5±7.8	<0.001	15.7±4.9
Mean BMI (kg/m <sup>2</sup> )	16.1±2.9	15.4±2.6	> 0.05	16.7±4.9
Mean HbA1C (%)	11.5±1.7	10.9±2.1	> 0.05	9.6±1.9
Mean SBP (mmHg)	92.8±9.5	85.7±10.1	<0.05	87.3
Mean DBP (mmHg)	64.4±8.3	59.0±7.7	< 0.05	60.2

FHD= Family history of diabetes; BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; FHT1D = Family history of type 1 diabetes

As shown in Table 3, majority of the affected family members were second-degree relatives. Multiple number of family members were affected in 41.4% of cases (Figure 1). In two (6.9%) of the 29 subjects, both mother and father were affected. Both first- and second-degree relatives were affected in 8 (27.6%) of the 29 subjects with positive family history of diabetes. All three degrees (i.e., first-, second- and third-degree) of relatives were affected in 2 (6.9%) of the 29 subjects. Regarding affected siblings of parents (uncles and aunts), 7 (24.1%) were paternal uncles, 3 (10.3%) paternal aunts, one (3.4%) maternal

uncle and 4 (13.8%) maternal aunts. The proportion of subjects with affected grandparents was 27.6% (8/29). Among them, 4 (13.8%) were maternal grandmother, 3 (10.3%) were maternal grandfathers and 1 (3.4%) was paternal grandmother. None of the affected relatives was a paternal grandfather. As shown in Figure 2, majority of the subjects with positive family history were in average family history risk category. The age of the subjects did not differ with family history risk categories. One of the subjects aged 9 years had a father with type 2 diabetes (who required switching to insulin therapy) and

three elder sisters with prediabetes. Information on type of diabetes in the affected family members was available in 22 (75.9%) of the 29 subjects with positive

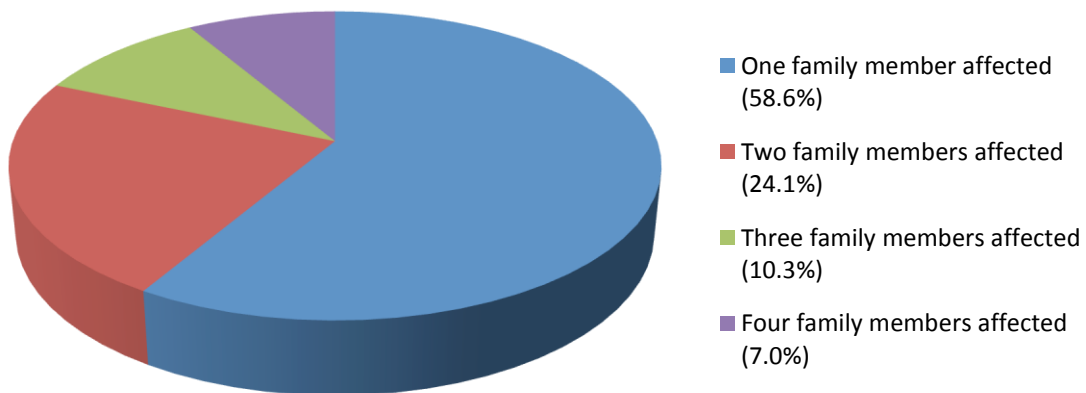
family history of diabetes mellitus. Among the affected family members in whom information on their diabetes status was available, 19 (86.4%) had type 2 diabetes and only 3 (13.6%) had type 1 diabetes.

**Table 3. Distribution of study subjects according to which family member is affected**

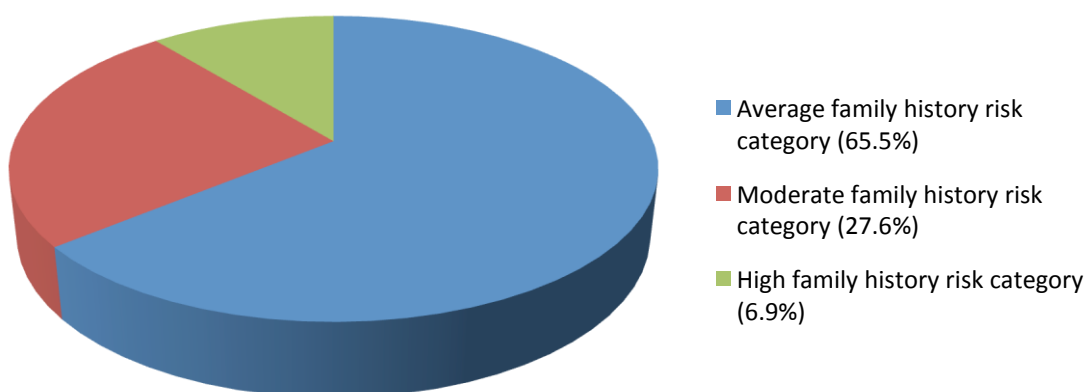
<i>First-degree relatives</i>	Number (n=42*)	Frequency (%)
Father	7	16.7
Mother	10	23.8
Sibling- brother	1	2.4
Sibling- sister	0	0.0
Siblings- brothers plus sisters	1	2.4
Total	18	42.9
<i>Second-degree relatives</i>		
Grandparents	7	16.7
Siblings of parents (uncles/aunts)	15	35.7
Total	22	52.4
<i>Third-degree relatives</i>		
Great grandparents	0	0.0
First cousins	0	0.0
Other relatives of parents	2	4.8
<b>Total</b>	<b>2</b>	<b>4.8</b>

\*Some of the subjects have more than one family member affected.

**Figure 1: Distribution of number of family members affected.**



**Figure 2: Distribution of family history risk category among subjects with positive family history of diabetes mellitus**



## **Discussion**

Data from the present study indicate that at least four out of every ten (44.6%) children and adolescent with type 1 diabetes have a positive family history of diabetes mellitus. This frequency is higher than the 24.1% reported from Finnish Paediatric Diabetes Register [21] but lower than 58.3% and 74.0% reported from Oman [21] and Saudi Arabia [27], respectively. The observed variation in frequency may be explained by the fact that a family history of a disease is reflection of the consequences of inherited genetic susceptibility, shared environmental factors and common lifestyle behaviours [6,7]. The magnitude of the contribution of each of these predisposing factors vary from country to country, accounting for the observed differences in frequencies of positive family history. The public health implication of the prevalence of positive family history of diabetes mellitus found in the present study is that true sporadic cases of newly diagnosed type 1 diabetes is less than 60% in our environment. In addition, the frequency of positive family history of diabetes was significantly higher in Gombe (Northern Nigeria) than Lagos plus Benin City (Southern Nigeria). The common practice of consanguinity in marriages in the northern part of Nigeria in contrast to the southern Nigeria may account for the higher frequency of positive family history of diabetes in the north [28]. This view is supported by literature which has documented that a consanguineous couple is at increased risk for disorders inherited either as autosomal recessive or multifactorial traits [29]. Diabetes mellitus is inherited as a multifactorial trait. We encourage other researchers who have the necessary data to follow up on our hypothesis by using a larger sample size

involving more healthcare institutions in Nigeria.

We found that in over one half (53.7%) of the subjects, second-degree relatives were affected. This is in keeping with 54.6% reported from Finland [10]. In contrast, a study in Saudi Arabia reported that 52.5% of affected family members were first-degree relatives [27]. The higher frequency among first-degree relatives found in Saudi Arabia compared to our study may be due high frequency of consanguinity in Saudi Arabian families. In the same study [27], the authors reported consanguineous union in 40.0% of all admitted children's parents. In consonance with some studies [6,10], we found that a larger proportion of maternal relatives than paternal relatives were affected. Although we do not have any readily available explanation for this finding, differential expression of inherited susceptibility genes in the paternal and maternal generations (i.e., genomic imprinting) has been proposed [30]. In the present study, multiple number of family members were affected in at least, four out of every ten cases (41.4%). This is in keeping with the results of other studies [10,11,23]. The high proportion of multiple family members found in our study is worrisome because for any given individual, both prevalence and odd ratio estimates are known to be significantly increased with number of relatives affected by diabetes [5,6,11]. Our data indicate that majority (86.4%) of the affected family members had type 2 diabetes. Therefore, the high proportion of family history of type 2 diabetes along with multiple family members affected in our study is of public health importance.

Concerning stratification into family history risk categories, we found that one in 16



cases (6.9%) were in the high family history risk category. This finding agrees with 7.5% found in USA (using the same criteria for definition as in the present study) [5]. In the same study, the authors reported a moderate risk category of 22.7% and an average risk category of 69.8% [5], both of which are comparable with 27.6% and 65.5%, respectively found in our study. In contrast, the results of a study in China revealed frequencies in a reversed order. In that study, the reported frequency of the family history risk categories was high 32.7%, moderate 20.1% and average 8.4%, respectively [11]. The reason for the differences in proportion of family history risk category in our study compared with the Chinese study [11] is not clear. However, it may be related to differences in the criteria used in defining the family history risk category. The USA study [5] as well as the present study used the criteria suggested by Scheuner et al [25] which considered both first- and second-degree relatives while the Chinese study [11] used only the first-degree relatives. Indeed, the authors mentioned limiting family history to only first-degree relatives as a drawback of their study [11]. The public health importance of family history risk category is that it is significantly related not only to level of islet  $\beta$ -cell dysfunction but also a significant and independent rank correlation with prevalence of diabetes in individuals [5,11].

Presence of family history of diabetes was associated with a relatively less severe metabolic decompensation at first diagnosis. The evidence is reflected in the significantly lower proportion of subjects with impaired consciousness and ketoacidosis in the group with positive compared to negative family history. Similarly, subjects with positive family history of diabetes had shorter duration of symptoms before diagnosis.

This trend is in consonance with the reports of previous studies [10,31]. This finding may be due to better awareness of the parents with regard to early symptoms of type 1 diabetes, resulting in a relatively early diagnosis and initiation of treatment. This view is reinforced by the shorter duration of symptoms in patients with positive compared to negative family history of diabetes found in our study. The present study did not investigate for the association between high blood pressure and family history of diabetes. It is possible that the tendency for high blood pressure in patients with positive family history of diabetes is due the fact that both hypertension and diabetes mellitus are inherited as a multifactorial trait.

Some limitations of the present study need to be considered. First, our inability to encourage the subjects/parents to contact relatives to confirm family history of at least three generations of relatives. This probably would have increased the number of affected third-degree relatives found in this study. This view is supported by the finding in a study in USA where 2.7% and 2.0% of men and women, respectively lacked knowledge of family history of diabetes [6]. Secondly, we did not assess the prevalence of diabetes in various family history risk categories. Our study did not have a control group because the study was largely retrospective. The small number of patients did not allow for adequate comparison of patients with positive family history of type 1 diabetes and type 2 diabetes. Despite these limitations, our study is the first to provide an insight into the prevalence and characteristics of family history of diabetes mellitus in the paediatric age group in Nigeria. Therefore, it can serve as part of the public health tool for screening and

preventive programmes in paediatric diabetes mellitus.

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