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Characteristics and Glycaemic Control of Early onset Type 2 Diabetes Mellitus in Children before 10 years of age in Bangladesh: A Retrospective Analysis

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Abstract

Introduction: Type 1 diabetes has traditionally been the most common form of diabetes in children. However, there is a growing rise in type 2 diabetes, which, although still rare under 10 years of age, is increasingly seen in high-risk populations.

Objective: To evaluate the clinical characteristics and glycaemic control of children diagnosed with T2 D before the age of 10.

Methods: A retrospective review was conducted of electronic medical records of children diagnosed with T2 D before age 10 at the BADAS Paediatric Diabetes Care and Research Center, BIRDEM Hospital, Bangladesh, over a 12-year period. Baseline characteristics and glycaemic outcomes were analyzed.

Results: A total of 55 children (median age 9.0 [8.0–9.5] years) were diagnosed with T2D; 80.0% were female. All had a family history of diabetes, and 47.2% had a history of gestational diabetes. Acanthosis nigricans was noted in 74.5% of cases. The median BMI was 23.0 [20.3-25.8] kg/m2, with the majority being overweight or obese. Non-alcoholic fatty liver disease was observed in 31%, and More than 80.0% required insulin, either alone or in combination with metformin at diagnosis. Median C-peptide was 2.2 [1.5–3.0] ng/mL, median HbA1c at diagnosis was 11.4 [8.7–13.4]%. At six months, glycaemic improvement was noted with median HbA1c reduced to 7.7 [7.0–9.3]%, and 22.2% achieved optimal glycaemic control (HbA1c ≤6.5%).

Conclusions: T2 D can occur in children younger than 10 years in high-risk populations. Early identification and intensive management are critical to achieving better glycaemic outcomes in this vulnerable age group.

Keywords: T2 diabetes, ealy onset, Bangladesh, glycaemic control

Introduction

Type 1 diabetes has traditionally been the most prevalent form of diabetes among children. However, there is a notable rise in type 2 diabetes (T2D) in this age group, reflecting a broader global health challenge [1]. This increase in youth-onset T2D is intimately tied to the escalating epidemic of childhood obesity and increasingly sedentary lifestyles. Although the diagnosis of youth-onset T2D is extremely low among pre- pubertal children however, it has been reported in children younger than 10 years. In the pediatric population, the onset of type 2 diabetes is most often around the adolescence period, however, there are rare reports of type 2 diabetes developing in children as young as 5 and 8 years of age [2, 3]. The US SEARCH for Diabetes in Youth Study reported that children younger than 10 years comprised 3.6% of newly diagnosed T2 D cases [4]. Similarly, a Canadian study found that 8% of newly diagnosed T2 D children were less than 10 years of age [5]. Overall, the SEARCH study observed a 30.5% rise in T2 D prevalence among youth, with 2.4% of cases occurring in those under 10 years old [6]. Given the significant` impact of risk factors such as obesity, family history, and ethnicity, T2D should be considered in children with these risk factors regardless of their age or the presence of symptoms [7]. Notably, the risk of pediatric T2D is greatly influenced by obesity, particularly the accumulation of visceral fat, which worsens insulin resistance, a key feature of the disease.

Children with a family history of T2D are also at increased risk. Diabetes Canada recommends screening for T2 D in prepubertal children with three or more risk factors and in pubertal youth with two or more risk factors [8]. A recent study conducted at our center in Bangladesh revealed that 10 (14.7%) of 68 T2D patients were diagnosed before the age of 10 [9]. This study aimed to assess the baseline clinical, demographic, and laboratory characteristics, as well as the glycemic control and treatment approaches for children and adolescents with T2 D diagnosed under the age of 10 at our institution.

Methods

A retrospective review of electronic medical records was conducted for children diagnosed with type 2 diabetes mellitus (T2D) at the BADAS Pediatric Diabetes Care and Research Center in BIRDEM Hospital over a span of 12 years. Demographic data collected included date of birth, sex, ethnicity, city and province of residence at diagnosis, date of diagnosis, age at diagnosis, etc.

Clinical parameters

The study focused on children and adolescents under 10 years old who were newly diagnosed with T2D. Diagnosis was made by local investigators based on a comprehensive evaluation of clinical features and medical history. Criteria for diagnosis included overweight or obesity, initial insulin requirements for blood glucose management, gradual onset or asymptomatic presentation, presence of acanthosis nigricans, dyslipidemia, and a family history of the disease. The classification of diabetes was based on ISPAD and local criteria [10, 11]. Body weight and height were measured by electronic scales and stadiometer respectively with subjects wearing light-weight clothing and without shoes. The body mass index (BMI) was calculated as weight in kilogram divided by square of the height in meter. Body Mass Index (BMI) was then calculated using the WHO standards for patients [12].

Biochemical and serological assessments included measurements of fasting blood glucose and glycated hemoglobin (HbA1c) levels at the time of diagnosis. Blood glucose was determined using an enzymatic colorimetric method with a multichannel auto-analyzer. HbA1c levels were assessed using the Clover A1c analyzer, employing a photoelectric method from Infopia Co. Ltd. C-peptide concentrations were measured from frozen samples using commercially available ELISA kits (IBL, Hamburg, Germany) [13].

Ethical considerations

Informed consent was obtained from the parents to use the data of the children and adolescents and the family members for research purposes. The study was approved by the Ethical Review Committee of the Diabetic Association of Bangladesh.

Statistical analysis

Data analysis was conducted using SPSS version 25.0. Descriptive statistics are presented as mean(±SD) scores for normally distributed data and median (interquartile range or range) for skewed data.

Results

Among a total of 928 cases, 55 (6%) were diagnosed before 10 years of age, with a median age of 9 [8-9.5] years over the 12-year period. Many of these patients were female (82%), residing in urban areas (56.3%), and came from higher socioeconomic backgrounds (71%) [Table 1]. A positive family history, either in a first- or second-degree relative, was reported in all patients, (Figure 1) with 47.2% of mothers having a history of gestational diabetes mellitus (GDM). Three patients were asymptomatic and were diagnosed incidentally at home due to obesity and a strong family history of diabetes [Table 2]. The median BMI was 23.0 [20.3-25.8] kg/m2, with the majority being overweight

or obese, while only 12.7% were of normal weight. The median BMI was 23.0 kg/m^2 [range: 20.3-25.8 kg/m^2], with most patients classified as overweight or obese, while only 12.7% had a normal weight. Signs of insulin resistance, including acanthosis nigricans, were observed in 74.5% of the patients. The median HbA1c at the time of diagnosis was 11.2% [range: 8.7-13.4%]. Additionally, 17 patients (30.9%) were diagnosed with non-alcoholic fatty liver disease, exhibiting mild to moderate hepatic steatosis. The median C-peptide level in this population was 2.2 [1.5-3.0 ng/ml], while the median vitamin D level was notably low at 9.4 [5.8-11.4 ng/ml] [Table 3].

Lifestyle modification was advised to all patients, with an emphasis on diet and exercise. Initially, more than 80.0% required insulin, either alone or in combination with metformin, for management of hyperglycemia. Treatment modalities included lifestyle counseling alone (20%), lifestyle counseling combined with insulin (76.3%), and lifestyle counseling combined with an oral agent (3.6%). Despite an increase in weight, there was a reduction in insulin dosage and a notable decrease in median HbA1c levels. After one year, 22.2% of patients achieved optimal glycemic control with HbA1c levels below 6.5%.

Discussion

The results of this study highlight the increasing prevalence of T2D in children under the age of 10. While T2D onset has been predominantly observed in adolescence, however, our findings reveal a concerning trend of earlier occurrences, especially among prepubertal children. This demographic group has been relatively understudied, resulting in limited data on children diagnosed with T2D.

Table 1: Demographic characteristics of newly diagnosed children and adolescents with Type 2 diabetes (n=55).

Parameter	Frequency (%)
Gender	
Male	10(18)
Female	45(82)
Area	
Urban	31(56.3)
Semiurban	14(25.4)
Rural	10(18.1)
Socioeconomic status	
Low	16(29)
Middle to high	39(71)
Family history of diabetes	
Yes	55(100)
No	0(0)
H/O GDM	
Yes	26(47.3)
No	29(52.7)

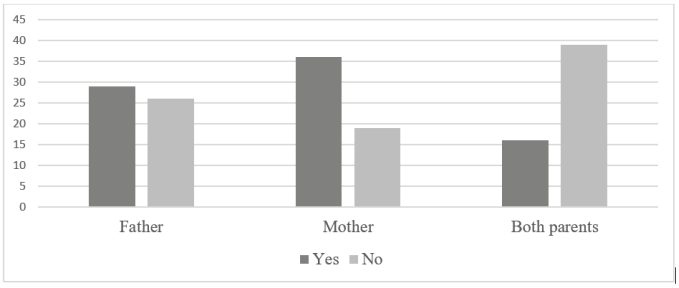

Figure 1: Family H/O diabetes in the patients (n=55).

Table 2: Clinical and biochemical characteristics of patients (n=55)

Parameters	Median
Age at diagnosis (yrs)	9.0[8.0-9.5]
Age at registration (yrs)	9.1[8.5-9.8]
Blood Pressure (mm of Hg)	
Systolic	100[90-110]
Diastolic	60[60-70]
FBS (mmol/ L)	14.8[8.4- 17.2]
HbA1c ((%) (mmol/mol)	11.2 [8.7-13.4] 99[72- 123]
C peptide (ng/dl)	2.2[1.5-3.0]
Vit D (ng/ml)	9.4[5.8-11.4]

Table 3: Clinical Characteristics of newly diagnosed children and adolescents with Type 2 diabetes (n=55).

Parameter	Frequency (%)
Symptoms	Frequency (%)
Typical symptoms	29 (52.7)
Atypical	23 (41.8)
Asymptomatic	3 (5.4)
Acanthosis nigricans	
Present	41(74.5)
Absent	14 (25.5)
BMI	
Normal weight	7 (12.7)
Overweight	29 (52.7)
Obese	19 (34.5)

There is a paucity of literature focusing specifically on children diagnosed with T2D during prepubertal ages, defined as 10 years or below. Additionally, many existing studies tend to merge these cases with those involving type 1 diabetes (T1D) [14, 15].

Notably, a substantial proportion of the identified cases were females, consistent with prior research suggesting a greater susceptibility among adolescent girls. Previous studies have indicated that adolescent girls face a higher risk of developing T2D compared to their male counterparts. Furthermore, research indicates that girls are more predisposed to developing childhood-onset diabetes, with the onset occurring earlier in both

prepubertal and post pubertal stages [16-19]. This predisposition, coupled with the observation that these cases predominantly originate from urban settings and higher socioeconomic backgrounds, suggests a plausible association between lifestyle factors and the early onset of T2 D. This predisposition, combined with the observation that these cases primarily arise from urban environments and higher socioeconomic backgrounds, suggests a likely association between lifestyle factors and the early onset of T2D. Moreover, the high prevalence of a positive family history of diabetes and a history of gestational diabetes among the mothers of these patients highlights a significant genetic predisposition to the disease.

Exposure to maternal diabetes—both pre-gestational and gestational diabetes (GDM)—along with maternal obesity and fetal over-nutrition, has been linked to an increased risk of developing T2D in offspring [20, 21]. Notably, in the TODAY cohort, one-third of youth with T2D were born to mothers with pre-existing diabetes or gestational diabetes (GDM) [22]. Overweight and obesity were prominent risk factors in our cohort, reflecting global trends that associate increased body mass index (BMI) with the onset of T2D in youth. Obesity is a well-established risk factor for the development of youth-onset T2D and plays a significant role in insulin resistance. Data from the United States indicate a strong inverse relationship between the age of diabetes onset and body mass index (BMI), with younger individuals tending to have higher BMI [23]. Correspondingly, the SEARCH study reported that 79.4% of youth with type 2 diabetes (T2D) were obese, and 10.4% were overweight, with similar proportions observed in European cohorts [24].

In our cohort, it is notable that all patients had C-peptide levels within the normal range. Assessing C-peptide levels in conjunction with clinical criteria is crucial for differentiating between T1D and T2D in pediatric cases [25]. Additionally, the presence of comorbidities like non-alcoholic fatty liver disease (NAFLD) and hypertension highlights the critical need for early detection and intervention in managing T2D within this population. While non-alcoholic fatty liver disease (NAFLD) is commonly observed in adults with type 2 diabetes, research indicates that it is also prevalent among adolescents with the condition [26]. One study found that nearly 30% of children with type 2 diabetes were affected by NAFLD [27].

Our treatment approach, encompassing lifestyle modifications, insulin therapy, and oral agents, reflects the multifaceted nature of managing T2D in children. While many patients required insulin therapy upon diagnosis, a significant proportion achieved optimal glycemic control through comprehensive treatment within a year. Vitamin D deficiency, prevalent among our cohort at diagnosis, warrants attention. Several studies in adults and children indicate that low vitamin D levels are associated with an increased risk of type 2 diabetes, particularly in individuals with obesity [28]. This highlights the importance of holistic care in addressing not only glycemic control but also associated metabolic disturbances.

The limitation of this study is the inability to perform antibody testing to differentiate between T1D and T2D definitively. Antibody testing is essential for accurately classifying diabetes types, particularly in pediatric cases. However, due to resource constraints or other practical limitations, antibody testing was not conducted in this study. Since antibody testing was not performed, there is a possibility of misdiagnosis or misclassification of diabetes types.

Moreover, it's crucial to note that antibody-negative idiopathic type 1 diabetes is also prevalent in Bangladesh, as evidenced by previous studies. This adds complexity to the classification process, as relying solely on antibodies may not always provide a clear distinction between T1D and T2D. While clinical and historical criteria may be valuable tools for diabetes typing, they may not be sufficient in all cases. Future studies should prioritize incorporating antibody testing to ensure proper classification of diabetes types and improve the validity of the results. Additionally, exploring alternative methods for diabetes typing in resource-constrained settings like Bangladesh could help address this limitation.

Conclusion

In conclusion, these findings emphasize the critical importance of early detection and management of type 2 diabetes mellitus T2D in children, particularly those at higher risk due to family history and lifestyle factors. Further research is imperative to elucidate the underlying mechanisms contributing to the rise in T2D and to develop more targeted interventions for prevention and management. Our study underscores the need for heightened clinical vigilance, urging clinicians to consider T2D even in younger children below 10 years lacking classic symptoms but presenting with risk factors.

Author Contributions: BZ, BA, KH and JN conceptualized and BZ wrote the paper. JN, BA and KA revised the text and BZ finally edited and approved the final manuscript.

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Ethical Approval and Patient Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Disclosure statement

The authors declare that they have no potential conflicts of interest relevant to this article.

Data availability: The data that supports the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy and ethical restrictions.

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