



Original Article

Pubertal Development of Children and Adolescents Living with Diabetes in Yaoundé (Cameroon)

Développement pubertaire des enfants et adolescents vivant avec le diabète dans la ville de Yaoundé (Cameroun)

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ABSTRACT

Background. Diabetes in children as a chronic disease, has a detrimental effect on staturponderal and pubertal development when not properly controlled. The aim of this study was to evaluate pubertal development in adolescents living with diabetes. **Method.** We carried out a cross-sectional comparative study at the Yaoundé Central Hospital and at the Mfou High School in Cameroon. Adolescents aged 9 to 18 years with diabetes were included, regardless of gender. They were compared to non-diabetic adolescents from the same age group. Participants who had any chronic conditions besides diabetes were excluded. Each participant was examined in the presence of the parent at their convenience. Pubertal development was assessed through physical examination and graded according to Tanner's stage. For statistical analysis, we used Chi-2 and exact Fisher tests to compare both groups. The significance level was $p < 5\%$. **Results.** We enrolled 43 children with diabetes and 185 children in the control group. The mean age of children with diabetes was 15.1 ± 2.3 years versus 13.9 ± 2.2 years for the control group. The mean HbA1c was $8 \pm 2.1\%$. Underweight was found in 41.7% of children with diabetes versus 9% in the control group of the same age ($p < 0.0048$). There was no difference between the 2 groups in the onset of puberty ($p = 0.1953$). Delayed puberty was present in 55.8% among patient living with diabetes, and it was more present in girls compared to boys (66.6% versus 48%). Ketoacidosis was associated with delayed puberty (0.0001). **Conclusion.** Delayed puberty is more common in the diabetic population and is strongly associated with ketoacidosis.

RÉSUMÉ

Introduction. Le diabète chez l'enfant en tant que maladie chronique a un impact délétère sur le développement statur-pondéral et pubertaire lorsqu'il n'est pas bien contrôlé. L'objectif de ce travail était d'évaluer le développement pubertaire chez les adolescents vivant avec le diabète et suivis à l'Hopital Central de Yaoundé. **Méthode.** Il s'agissait d'une étude transversale descriptive et comparative à l'Hôpital central de Yaoundé et au Lycée de Mfou. Etaient inclus les adolescents de 9 à 18 ans, indépendamment du sexe et ayant un diabète et les adolescents non diabétiques de la même tranche d'âge. Chaque participant était examiné en présence du parent s'il le désirait. Le développement pubertaire était évalué à l'examen physique et classé selon le stade de Tanner. Les analyses statistiques, ont été faites avec les tests de Chi-2 et de Fisher exact. Le seuil de significativité était $p < 5\%$. **Résultats.** Nous avons recruté 43 enfants diabétiques contre 185 enfants dans le groupe contrôle. L'âge moyen des enfants diabétiques était de $15,1 \pm 2,3$ ans contre $13,9 \pm 2,2$ ans dans le groupe témoin. L'HbA1c moyenne était de $8 \pm 2,1\%$. Le déficit pondéral était retrouvé chez 41,7% des enfants diabétiques contre 9% chez les témoins de la même tranche d'âge ($p < 0,0048$). Il n'y avait pas de différence entre les 2 groupes quant au démarrage de la puberté ($p = 0,1953$). La prévalence du retard pubertaire était de 55,8% chez les diabétiques, il touchait plus les filles (66,6%) que les garçons (48%) ($p = 0,022$), contre 22,7% chez les témoins. L'acidocétose était associée au retard pubertaire (0,0001). **Conclusion.** Le retard pubertaire est plus fréquent chez le diabétique et est fortement associé à l'acidocétose.

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HIGHLIGHTS**What is already known on this topic**

Poorly controlled diabetes in children can affect their normal development. Little is known about this topic in Cameroon.

What question this study addressed

Pubertal development of Cameroonian children living with diabetes.

What this study adds to our knowledge

Although the onset of puberty in Cameroonian children with diabetes is similar to that of the general population, delayed puberty is more common in diabetic children. Moreover, ketoacidosis is associated with delayed puberty in children living with diabetes.

How this is relevant to practice, policy or further research.

This study stresses the importance of good control of childhood diabetes for normal pubertal development and prevention of ketoacidosis.

INTRODUCTION

Diabetes in children is a chronic disease with severe complications on the quality of life of the child and his family, as well as on the child's current and future health [1]. According to studies carried out on children living with diabetes, the earlier the onset of diabetes, the greater the immediate risk of developing a hyperglycaemic or hypoglycaemic coma. In resource-limited countries such as Cameroon, mortality among children living with diabetes remains high despite the free supply of insulin in this patient group [2]. This is related to the environment, the behavior of the population but also the organization of the health care systems. While the long-term complications of chronic hyperglycemia are metabolic and cardiovascular and account for most of the public health severity of the disease [1]. Diabetes as a chronic disease has an impact on the pubertal development, weight, height and psychological state of young patients [3,4,5]. There could be an altered quality of life and a higher frequency of anxiety rate[5]. Diabetes in children and adolescents, is considered as a factor that potentially affects the onset of male and female puberty but not pubertal development and maturity [6]. The earlier its onset, the longer and more severe the disease and the greater the impact on growth and pubertal development. The aim of our work was to evaluate the pubertal development of adolescents living with diabetes in a cohort of patients living with diabetes followed at the Yaoundé Central Hospital.

METHODS**Study design and setting**

We conducted a cross-sectional, comparative study over a 5-month period from December 2020 to April 2021. The study took place at the National Obesity Center at the Yaoundé Central Hospital (HCY) and at the Mfou Technical High School in Yaoundé.

Participants

Our study population consisted of young children and adolescents of both genders aged between 9 and 18 years. The children living with diabetes were selected from the

population of diabetic patients followed at the Yaoundé Central Hospital. The control subjects were selected from the Mfou technical high school.

- Inclusion criteria: We included consenting boys and girls living with diabetes, aged 9 to 18 years, and whose parents' or legal guardian's assent was received. These patients were compared to young people aged between 9 and 18 years of both genders, non-diabetic, regularly enrolled in school, whose authorizations for enrolment had been issued and signed by the school administrative officials and parents (and/or legal guardian)
- Exclusion criteria : We excluded from our study:
 - School adolescents without diabetes but with other chronic diseases. As well as diabetic patients with other chronic diseases reported before the onset of puberty.
 - Adolescents with abnormal pubertal development before the discovery of diabetes.

Sampling

We conducted a non-probability consecutive exhaustive sampling.

Procedure*Administrative procedure*

We obtained authorization from the director of Mfou technical high school to conduct the study within the school. Each child had to have prior parental or legal guardian consent to participate in the study. Information was collected through questioning and review of medical records for diabetic children.

Enrollment of participants was done as follows: patients living with diabetes were recruited during routine visits. For the control subjects, an announcement was made at the assembly by the high school principal; an informative note explaining the purpose of the study was given to each student to be signed by his/her parent or legal guardian. This was to obtain permission for the student to participate in the study. Ethical clearance n°527 was obtained from the Institutional Ethics and Research Committee (CIER) of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I.

Each participant was interviewed and then examined in the presence of their parent at their convenience. The children from the high school were examined in the high school infirmary.

During the interview, the following information was collected from both groups: age, sex, and marital status of the parents. For children living with diabetes, the following information was collected: age of onset of diabetes, duration of diabetes, number of hypoglycemia and ketoacidosis, and glycemic control evaluated by glycosylated hemoglobin. We also search for the presence of documented chronic complications.

Evaluation of pubertal development

Pubertal development was assessed through questioning and completing by physical examination. The physical examination was done in a closed room. It consisted in describing the secondary sexual characteristics in the two groups of participants. This allowed us to classify the pubertal development according to its evolution thanks to a sexual maturity rating by Tanner [7,8].

In boys, the following informations were collected during the interview: the age of puberty onset: the age of increase in testicular volume and/or size of the penis, and the age of vocal molt. The volume of the testicle was evaluated with an orchidometer, the volume obtained was classified from V1 to V5. V1 corresponded to a testicular volume of less than 4ml, V5 the testicular volume is of adult size with hyperpigmented and wrinkled scrotal skin (Figure1). In girls, the age of onset of breasts and menarche was recorded. Breast development was classified from B1 to B5. B1 corresponded to the absence of breasts and B5 corresponded to adult size breasts with hyperpigmented areola, raised nipple and not in the same plane as the mammary gland (figure1).

In both sexes, pubic hair was classified from P1 to P5 according to the quantity of pubic hair. P1 corresponds to an absence of hair in the prepubertal infantile stage and P5 corresponds to a well-filled hair in the adult stage.

At the end of the clinical examination, puberty could be considered normal, delayed or precocious.

Normal Puberty: puberty was considered normal in boys if the testicular volume started to increase at 9.5 years of age (an increase of more than 4ml) and reached a

maximum volume of > 25ml over the following 4 years, around 13.5 to 14 years of age. In girls, normal puberty was defined by the appearance of breasts from the age of 8 years. Acquisition of the Tanner stage 5 to 14 years [9].

Delayed puberty: It was defined in boys if there was no increase in testicular volume (< 4 ml or length < 25 mm) beyond 14 years. In girls if absence of breast development at 13 years of age or absence of menses (primary amenorrhea) at 15 years of age [9].

In both sexes, pubertal delay was considered to be the cessation of pubertal progression for more than 2 years, or TANNER stage < 5 at 14 years.

Precocious puberty: precocious puberty has been considered when signs of puberty appear before 8 years of age in girls and before 9.5 years of age in boys. And in girls: appearance of breasts from 8 years of age. Acquisition of the Tanner stage 5 to 14 years [9].

Factors influencing pubertal development : We searched for factors influencing pubertal development in diabetic patients based on data from the literature (7) (11). These were related to the poor control of diabetes. Each factor was analyzed according to whether puberty was normal or delayed.

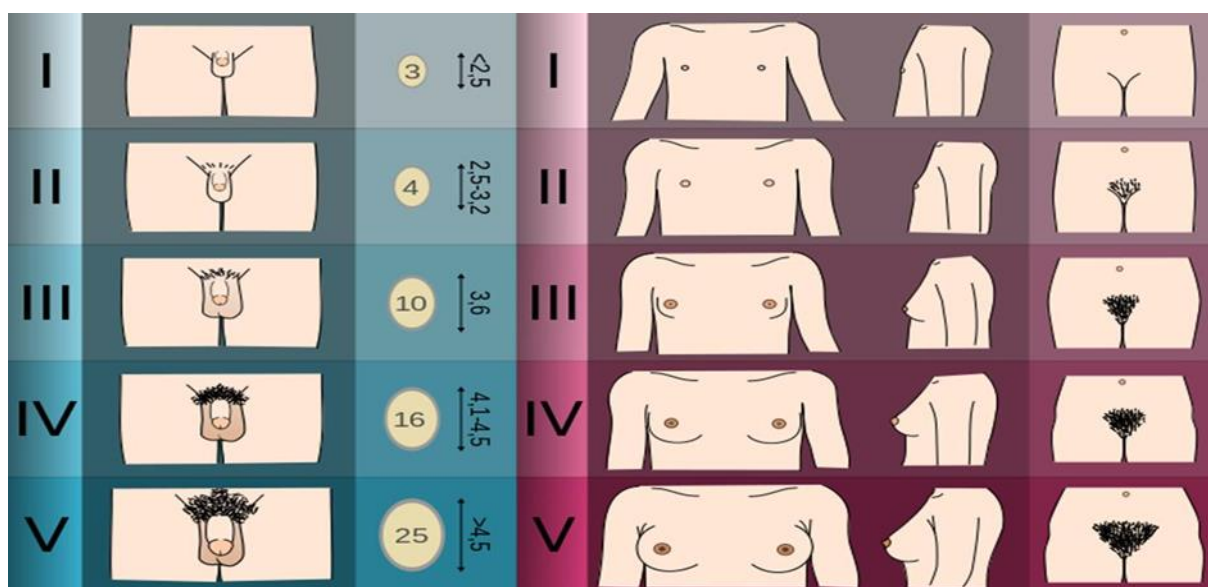


Figure 1 : Development of sexual characters in girls and boys [9] .

Age	BMI						p-value
	<16	[16-17,5[[17,5-18[[18-25[[25-30[[30-35[
9-13 years							0.004
Diabetic	2	5	0	4	0	1	
n (%)	(16.7)	(41.7)	(0)	(33.3)	(0.0)	(8.3)	
non diabetic	10	8	9	60	2	0	
n (%)	(11.2)	(9)	(10.1)	(67.4)	(2.3)		
14-15 years							0.172
Diabetic	2	1	0	6	0	0	
n (%)	(22.2)	(11.1)	(0)	(66.7)	(0.0)	(0)	
Non diabetic	1	6	7	35	0	1	
n (%)	(2)	(12)	(14)	(70)		(2.0)	
16-18 years							0.915
Diabetic	0	0	2	20	2	0	
n (%)	(0)	(0)	(8.3)	(83.3)	(8.3)	(0)	
Non diabetic	1	2	5	33	5	0	
n (%)	(2.2)	(4.4)	(10.9)	(71.7)	(10.9)	(0)	

Statistical analysis

SPSS version 26.0 and Excel were used to perform the data entry mask and statistical analysis of the data. The quantitative variables were expressed as means, with standard deviation. To compare the proportions, we used the Chi-square and Fisher exact tests. A P-value < 0.05 was used as the threshold of significance.

RESULTS

We enrolled a total of 43 patients living with diabetes (25 boys and 18 girls) and 185 non-diabetic children (126 girls and 59 boys).

Socio-demographic characteristics of participants

Distribution according to age

The average age of the diabetic children was 15.1 ± 2.3 years and 14 ± 2.2 years in the nondiabetic children.

Marital status of parents

Most parents were married in both groups, in diabetics (44%) and non-diabetics (36%). P-value = 0.02.

Anthropometric parameters

Body mass index by age group in the "diabetic" and "non-diabetic" study population

Overall, in the age groups above 13 years, the BMI was normal between 18 and 25 kg/m² in diabetic children. There was no significant difference between the two population groups. For all age groups in non-diabetic children, the BMI was normal. However, among diabetic children in the younger age groups [9-13 years], 33.3% had a normal BMI compared to 67.4% of non-diabetic children in the same age group (P=0.004). Table 1.

History of diabetes

Age of onset and duration of diabetes

The mean age at discovery of diabetes was 12 years. The average duration of diabetes was 3 years. With a maximum duration of 9 years.

Glycaemic control:

The mean value of glycated hemoglobin was $8.03 \pm 2.1\%$. HbA1c was around 7% in 39% of patients.

Acute complications

a. Severe hypoglycemia

Severe hypoglycemia was observed during diabetes follow-up in 18% of patients.

b. Diabetic ketoacidosis

During diabetes follow-up, 40% of patients had developed diabetic ketoacidosis.

Description of pubertal development in study population

Pubertal development in girls with and without diabetes

Pubertal development in girls was similar in both groups. It is noted that the appearance of breasts was more marked around the age of 11 to 13 years in both diabetic and non-diabetic girls. After the age of 16, in both groups, all participants had already developed breasts. There was no significant difference between thelarche and the presence or absence of diabetes (P=0.2764). The majority of

diabetic girls had observed menarche around the age of 9 to 10 years compared to non-diabetic girls where menarche occurred mostly in the 11–13-year age group. After 16 years, all girls had already had their first menarche in both groups (Table 2).

Pubertal development in boys with and without diabetes

In boys, the onset of pubertal development in both groups was generally similar. The increase in testicular volume began in the majority of cases (60%) between [11-13 years] in both diabetic and non-diabetic boys. However, vocal molt occurred more rapidly in the non-diabetic boys, occurring in the age range [11-13 years] compared to the diabetic boys where it occurred around 14-16 years (P<0.0004) (Table 3).

Prevalence of delayed puberty and the different Tanner's stage in diabetic and non-diabetic girls and boys

There was a delay in pubertal development in 12 diabetic boys and 12 diabetic girls. The prevalence of delayed pubertal development was 55.8%, in diabetes patients compared with a prevalence of 22.7% in the non-diabetic group.

▪ In the boys' group

In the [14-15 years] age group of diabetic children, there were 4 children out of 7 (44.4%) with delayed puberty which stagnated at TANNER stage 2 and 3. TANNER stage 4 was the most represented in this age group among non-diabetic children.

In the [16-18 years] age group of diabetic children, there were 8 children with pubertal development in TANNER stage 4 considered here as delayed puberty. In the non-diabetic group, most children had TANNER stage 5.

▪ In the girls' group

In the [9-13 years] age group of diabetic children, there were 2 out of 7 children (16.7%) who had not yet started puberty were classified as B1P1 according to Tanner. The majority of non-diabetic girls, on the other hand, had already reached TANNER stages B2P2 and B3P3 in this age group.

In the [14-15 years] age group of diabetic girls, there was 1 out of 3 girls with B3P3, while the majority of non-diabetic girls were already at least B4P4 in the same age group.

In the age group [16-18 years] of diabetic girls, 9 children had delayed puberty, of which 6 were in TANNER stage B3P3 in 6 girls and 3 girls in TANNER stage B4P4. The majority of non-diabetic girls in this age group had TANNER stage 5 (Table 4).

Correspondence of the TANNER stage with the duration of diabetes

The distribution below shows that, in both sexes, the maximum TANNER stage (4 and 5) is reached for an average duration of diabetes of less than 5 years. After more than 5 years of diabetes evolution, we find a distribution of TANNER classified as stage 4, 3 or even 2 in some children. In girls the development of TANNER seems to be more delayed (stage 2 and 3) than in boys when the duration of diabetes is more than 5 years. (Figure 2)

Table 2: Description of pubertal development in girls with and without diabetes

	Diabetes	Non Diabetes	P value
Age at telarche n (%)			0.2764
9 – 10	4 (23.5)	48 (40)	
11 – 13	12 (70.6)	68 (56.7)	
14 – 15	1 (5.9)	4 (3.3)	
16 – 18	0 (0)	0 (0)	
Age of onset of pubic hair growth n (%)			< 0.0001
9 – 10	14 (87.5)	33 (29.5)	
11 – 13	2 (12.5)	75 (67)	
14 – 15	0 (0)	4 (3.6)	
16 – 18	0 (0)	0 (0)	
Age at menarche n (%)			< 0.0001
9 – 10	9 (60)	3 (3.7)	
11 – 13	6 (40)	57 (70.4)	
14 – 15	0 (0)	21 (25.9)	
16 – 18	0 (0)	0 (0)	

Table 3: Description of pubertal development in boys with and without diabetes

	Diabetes	Non Diabetes	P value
Age of onset of testicular size increase n (%)			0.1953
9 – 10	1 (4.3)	10 (18.2)	
11 – 13	14 (60.9)	33 (60)	
14 – 15	8 (34.8)	12 (21.8)	
16 – 18	0 (0)	0 (0)	
Age of onset of pubic hair growth n (%)			0.0002
9 – 10	13 (59.1)	8 (14.8)	
11 – 13	9 (40.9)	36 (66.7)	
14 – 15	0 (0)	10 (18/5)	
16 – 18	0 (0)	0 (0)	
Age of onset of penis size increase n (%)			0.0011
9 – 10	12 (52.2)	10 (17.9)	
11 – 13	11 (47.8)	30 (53.6)	
14 – 15	0 (0)	16 (28.6)	
16 – 18	0 (0)	0 (0)	
Age of mute n (%)			0.0004
9 – 10	1 (5.3)	5 (9.3)	
11 – 13	2 (10.5)	31 (57.4)	
14 – 15	16 (84.2)	18 (33.3)	
16 – 18	0 (0)	0 (0)	

Table 4: TANNER stage classification by age in diabetics and non-diabetics

Variables	Boys					Girls				
	G1P1	G2P2	G3P3	G4P4	G5P5	B1P1	B2P2	B3P3	B4P4	B5P5
9-13 ans										
Child with diabetes n (%)	0 (0)	4 (33.3)	0 (0)	1 (8.3)	0 (0)	2 (16.7)	2 (16.7)	2 (16.7)	1 (8.3)	0 (0)
Child without diabetes n (%)	1 (1.1)	6 (6.7)	8 (9)	6 (6.7)	1 (1.1)	7 (7.9)	31 (34.8)	25 (28.1)	1 (1.1)	2 (2.3)
14-15 ans										
Child with diabetes n (%)	0 (0)	1 (11.1)	3 (33.3)	2 (22.2)	1 (11.1)	0 (0)	0 (0)	1 (11.1)	1 (11.1)	0 (0)
Child without diabetes n (%)	0 (0)	2 (4)	4 (8)	10 (20)	5 (10)	0 (0)	5 (10)	8 (16)	16 (32)	0 (0)
16-18 ans										
Child with diabetes n (%)	0 (0)	0 (0)	0 (0)	8 (33)	6 (25)	0 (0)	0 (0)	6 (25)	3 (12.5)	0 (0)
Child without diabetes n (%)	0 (0)	0 (0)	3 (6.5)	4 (8.7)	10 (21.7)	0 (0)	1 (2.2)	8 (17.4)	9 (19.6)	11 (23.9)

Factors influencing pubertal development in children with diabetes

The table below groups the potential factors influencing pubertal development.

Diabetes was unbalanced (HbA1c >7%) in 14 children (31.8%) with normal pubertal development versus 15

children (34.1%) with delayed pubertal development (P=0.37).

The duration of diabetes was greater than 5 years in 7% of children with normal TANNER stage versus 14% of diabetic children with pathological TANNER stage (P=0.62).

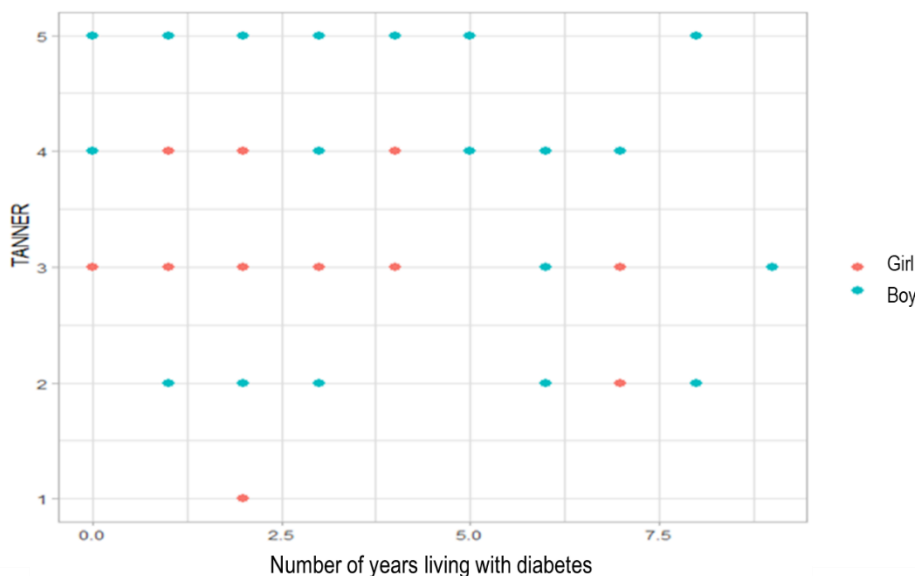


Figure 2: TANNER score according to the number of years lived with diabetes

Factors	Pubertal development according to Tanner’s stage		P-value
	Normal n (%)	Delayed n (%)	
Gender			0.02
Girl	6 (13)	12 (26.1)	
Boy	14 (30.4)	12 (26.1)	
Diabetes control			0.37
HbA1c < 7%	6 (13.6)	8 (18.2)	
HbA1c : [7-8%]	3 (6.8)	7 (15.9)	
HbA1c > 8%	11 (25)	8 (18.2)	
Diabetes onset			0.62
< 1 an	6 (14)	7 (16.3)	
]1-5 ans]	10 (23.3)	10 (23.3)	
>5ans	3 (7)	6 (14)	
Body Mass Index			
< 18	7 (15.6)	5 (11.1)	
]18-25]	12 (26.7)	17 (37.8)	
>25	1 (2.2)	2 (4.4)	
Hypoglycemia			0.19
No	17 (37)	17 (37)	
Yes	3 (6.5)	5 (10.9)	
Ketoacidosis			0.0001
No	12 (26.1)	14 (30.4)	
Yes	8 (17.4)	10 (27.1)	

Of the children with delayed pubertal development, 17 did not have severe hypoglycemia and 5 had severe hypoglycemia (P=0.19). Regarding diabetic ketoacidosis, among children with delayed pubertal development, 10 children had ketoacidosis versus 14 without ketoacidosis; this difference was statistically significant (P=0.0001). Body mass index was normal in 17 children with pathological TANNER, while 5 children were underweight and 2 children were overweight (P=0.74).

DISCUSSION

The purpose of this study was to describe the pubertal development of children living with diabetes and to compare it with that of a control group. Our results showed that the prevalence of delayed puberty in children living with diabetes was 55.8% versus 22.7% in controls. Puberty seems to start at the same time in both groups, but sexual maturation is later in children living with diabetes.

Factors influencing delayed puberty were female gender and ketoacidosis.

Puberty onset

The onset of puberty in the 2 groups was similar. Data from the literature show this similar pattern of puberty onset in diabetics compared with the general population [4,6]. For decades, diabetes was considered a factor of poor prognosis in children and early mortality. However, with the means available and better control of diabetes, we have observed an increase in the life expectancy of these children and a more or less important influence on their height-weight development depending on glycemic control (11). Thus, it is right to observe a low incidence of delayed puberty. However, we found that in diabetic children, for a duration of the disease of more than 5 years, there was a higher incidence of delayed puberty compared to individuals of the same age group in the control group.

Several authors have reported that the earlier the onset of diabetes, the greater the impact on pubertal development (12). Indeed, the longer the subject is exposed to diabetes, the greater the risk of complications that may interfere with the overall development of the individual. This is also observed on the BMI, where a weight deficit is more frequent in the younger age groups of diabetic children under 13 years in our population (4). Persistent insulinopenia over the years of diabetes may be responsible for a decrease in GnRH pulsatility leading to functional hypogonadotropic hypogonadism but also to a delay in height and weight gain, as insulin is an anabolic hormone stimulating lipogenesis (4).

Maturation and completion of puberty

The final stage of puberty in girls is marked by menarche. In the past 2 decades, there is observed a trend to an earlier menarche in girls worldwide (13) (14). In our study, an onset of menarche was noted in 60% of diabetic girls in the 9–10-year age group, compared to 3.7% in the control group. However, in this age group, these girls in the DT group had an irregular and therefore possibly anovulatory cycle. It has been shown by several authors that diabetes can delay menarche when it precedes it (15),(16). Indeed, studies also explain the fact that menstrual cycle disorders exist in women with diabetes even if there is no amenorrhea. It is well known that insulin acts on the gonadotropic axis through its receptors in the hypothalamus (17). Therefore, insulin deficiency alters the pulsatility of GnRH and will therefore be responsible for amenorrhea in the insulinopenic diabetic girl (18). In addition to insulin receptors at the hypothalamic level, there are also insulin receptors in the ovaries, particularly in the theca and granulosa (19). Insulin is able to stimulate ovarian steroidogenesis as observed in PCOS (15). Insulinopenia requires an exogenous supply of insulin, sometimes in a multiple injection regimen. The exogenous insulin supply is chronic and exposes the body's cells to high doses, sometimes supraphysiological, since the mode of admission of the exogenous insulin escapes the first hepatic passage. These high doses of exogenous insulin can induce ovarian dysfunction, which is responsible, among other things, for menstrual cycle disorders. The literature shows that PCOS is also common in T1DM (15). This may be due either to the insulin resistance already observed more and more in this population, but also by the above-mentioned mechanism. Although there is an earlier onset of menarche in this age group, the irregularity may be a sign of possible hyperandrogenism that should be investigated over time. But also in our population the age of menarche from 9 years old could be the norm in our context, since European studies on larger samples and with ethnic diversity have revealed that menarche was generally earlier in black girls than in Caucasian girls (13).

We found that there could be a delay in the acquisition of the definitive stage of puberty around the age of 15–16 years in diabetic children when compared with controls where, at this age, pubertal maturation was already completed in both girls and boys. These observations were also made by Codner et al, who found that diabetic girls started puberty at the same age as the others (9.10 ± 0.28 years in the diabetic group vs 8.89 ± 0.11 years in the

control group, $p > 0.05$). However, they reached Tanner stages 4 and 5 later than the control group (4). Also, Attia and Elamin, reported the same observation in diabetic boys, where sexual maturation in diabetic boys (stage 5) was delayed and occurred at a mean age of 17.2 years (12) (20). Indeed, the mechanisms by which diabetes affects sexual maturity are not very clear, they are considered to be due to insulin deficiency, or to delayed release of GnRH, with a later release of testosterone and testosterone.

Another explanation would be due to glycemic imbalance which seems to be common in adolescence (21). At the age of puberty, there is a change in behavior often marked by denial of the disease in these children (22) (23). Many of them voluntarily stop their insulin treatment, exposing them to toxic ketoacidosis at the cerebral and hypothalamic level, which can alter the normal evolution of a puberty that has already begun.

Factors influencing puberty in children with diabetes:

L'HbA1c

Although studies have shown that the more unbalanced diabetes is, the more it can impact pubertal development (24) (25), our work did not show an association between glycemic control and pubertal development. Indeed, the average HbA1c in our population was 8%. We believe that this value may have been underestimated and does not biologically reflect the glycemic imbalance of this population. This may be explained by the fact that Cameroon is a highly endemic area for malaria and other parasitoses responsible for recurrent and chronic anemia. Anemia is known to falsely lower glycated hemoglobin.

Hypoglycemia

Among diabetic children with pathologic TANNER, only 5 children had had at least one severe hypoglycemia. The association between these two variables was not statistically significant ($P=0.1992$). In some studies, pubertal delay was associated with repeated hypoglycemia (20) (26). This different result from ours can be explained by the fact that although there is a subsidized management program in Cameroon for T1DM, insulins are not always available (availability and affordability) for all these patients. Therefore, these patients are more prone to ketoacidosis due to lack of insulin rather than hypoglycemia because some stopped taking the treatment for financial reasons.

Ketoacidosis

Ketoacidosis was significantly ($P=0.0001$) associated with pubertal delay in our study. Once again, insulin deficiency is responsible for this because of its action on GnRH pulsatility as described above but also because of the direct toxic action of ketone bodies at the level of the higher centers (15) (18).

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