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Research Article

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Chronic Complications of Type 1 Diabetes in Children

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Abstract

Introduction: *Chronic complications of type 1 diabetes are rare in children*

The aim of this work is to determine their prevalence in paediatric settings and the factors associated with them

Methodology: *This was a prospective study, conducted in two reference services in the management of childhood diabetes at the University Hospital of Dakar. We included all patients with type 1 diabetes under 20 years of age as recommended by the 2009 ISPAD.*

Results: *Of the 67 patients in our cohort, only 46 met the inclusion criteria. There were 19 boys and 27 girls. The average age was 11.57 years +/- 4.3 years. The average age of discovery was 8.71+/- 3.8 years. The average duration of the evolution was 34 months. Almost half of the patients had an average glycated hemoglobin greater than 9%.*

Growth retardation was severe in 17% and moderate in 11% of cases. Five patients (20%) had significant microalbuminuria and 5 (20%) had retinopathy, 3 with macular edema and 2 with diffuse microhaemorrhages.

Multivariate analysis of the different parameters studied showed that retinopathy was associated with high HbA1c values (p=0.043) and poor compliance (p=0.021). Kidney disease was only associated with poor adherence with p=0.0025.

Conclusion: *Chronic complications of T1D are not that uncommon, especially in our regions where management is not optimal. We suggest that they be detected around 10-11 years of age regardless of how long the diabetes progresses.*

Keywords: Type 1 Diabetes; Child; Chronic Complications

Introduction

Type 1 diabetes in children is increasingly diagnosed in our regions, but the data is still scarce and fragmented. Its prevalence is constantly increasing worldwide. In fact, according to the eighth edition of the IFD Diabetes Atlas, it affected around 1,106,200 young people under the age of 20 in 2017, including 586,000 young people under the age of 15 [1]. Vascular complications are rare in children; however, in regions where health care is not optimal, the risk of complications remains higher [2]. This is the case in our countries in particular, where access to insulin and other means of monitoring and managing T1D is often compromised. The work objective is to determine the prevalence of chronic complications of T1D in pediatric settings and the factors that are associated with them.

Methodology

It was a prospective, multicentric study, carried out in two reference services in the cost of diabetes in children: the pediatric service of the Abass Ndao Hospital Center and the Albert Royer National Children's Hospital Center. It took place over 1 year from November 2016 to November 2017. We included all type 1 diabetic patients followed for at least 6 months (to assess the impact on growth) and whose age was less than 20 years at the time of inclusion. Only patients whose guardians had refused to sign the consent for inclusion in the study were excluded. All patients were the subject of a statement of consent for inclusion in the study read and signed by their legal guardian. Patient clinical data were collected according to a pre-established questionnaire. Screening for diabetic retinopathy was carried out free of charge with the help of the ophthalmology department of the Abass Ndao Hospital Center. Screening for nephropathy was prescribed at the

patient's expense as part of their follow-up. We had studied socio-demographic data, the history of diabetes and its evolution under treatment. We looked for the following chronic complications:

- **Stunting:** for the screening of growth retardation we evaluated the size (age) index in all patients; and we had projected the result on the WHO curves. This allowed us to classify into three groups: Those who had a size / age index below the 3rd percentile (3P) were considered to be severely stunted, those who had a size (age) index between the 3rd and 10th percentile (between 3P and 10P) were considered to have moderate stunting, those who had a height (age) index greater than the 10th percentile were considered to have normal growth.

- **Diabetic Nephropathy:** we had detected it by determining the 24-hour microalbuminuria in patients fulfilling the age and scalability criteria according to the recommendations of ISPAD in 2009. The diagnosis was retained if the microalbuminuria was significant (albuminuria> 30 mg / 24h) at least 2 times.
- **Diabetic Retinopathy:** it was searched for by taking a fundus photograph in patients who met the ISPAD 2009 screening criteria.
- **Diabetic Neuropathy:** she was sought, in accordance with the screening criteria of ISPAD 2009 on the basis of interrogation and clinical examination in search of sensitivity disorders.
- **Macroangiopathy:** measuring blood pressure in all patients who met the age and scalability criteria for screening for macroangiopathic complications according to ISPAD 2009. Its measurement was reported on the WHO curves by size. Hypertension was defined as blood pressure above the 97.5th percentile.

Data entry was done with Excel software, and then the analysis was done with SPSS Statistics 25 software. The results were considered significant if the p-value was less than 0.05. The authors declare no conflict of interest in connection with this article

Results

Of the 67 patients in our cohort, only 46 met the inclusion criteria. There were 19 boys and 27 girls. The sex ratio was 0.70. The average age was 11.57 years +/- 4.3 years with extremes of 2 and 19 years and the age group between 11 and 15 years was more represented (46%) **(Table 1). I**n 84.78% of cases, there was no family history of type 1 diabetes. The average age of discovery was 8.71 years +/- 3.8 years with extremes of 1 and 17 years. In more than 28% of cases, diabetes was diagnosed before the age of 5. The average duration of evolution was 34 months. Half of the patients follow each other every 2 to 6 months. In 39% of cases, the patients had an irregular follow-up. The average glycated hemoglobin was 9.84% +/- 2.7%. Almost half of the patients (46%) had an average glycated hemoglobin greater than 9% (**Figure 1).** Stunting was severe in 17% and moderate in 11% of the cases. Among the 46 children, 25 were eligible for screening for diabetic nephropathy and 5 (20%) presented significant microalbuminuria. All of these patients were previously over 11 years of age and diabetic for at least two years (Table 2)**.** Of the 25 patients who met the screening criteria for diabetic retinopathy, 5 (20%) had retinopathy, including 3 with macular edema and the other 2 with diffuse microhaemorrhages. All patients with retinopathy were previously over 11 years of age and diabetic for at least two years **(Table 3).** None of our patients had neurological disorders. Blood pressure measurement and lipid balance were normal in all screened patients. Only one patient (patient 4) had both retinopathy and diabetic nephropathy.

Table 1: General patient data

Data		Number(n=46)	%
sex	Boys	19	41
	Girls	27	59
Age (ans)	0-5	3	7
	6-10	14	30
	11-15	21	46
	16-19	8	17
SEL	Poor	18	39
	Middle	10	22
	Good	18	39
Type of insulin	Human	30	65
	Analog	14	31
	Human and Analog	2	4
Insulin dose (ui/kg/j)	0,5-0,8	19	41,5
	0,8-1	8	17
	>1	19	41,5
Number of injections	4	16	35
	3	22	48
	<3	8	17

SEL: socioeconomic level

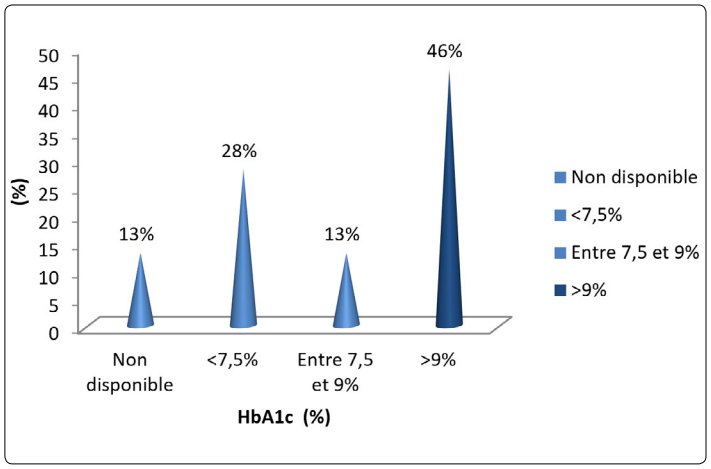

Figure 1: Distribution according to the means of glycated hemoglobin (HbA1c)

Table 2: Characteristics of patients with diabetic nephropathy

Parameters	Sex	Age (ans)	Diabetes duration (ans)	Type of insulin	Number of injections	follow up on (month)	HbA1c (%)
Patient 1	M	11	2	human	3	1	12,6
Patient 2	F	12	2	analog	4	2-6	9,2
Patient 3	F	16	2	analog	4	2-6	9,2
Patient 4	F	14	6	analog	4	2-6	10,3
Patient 5	M	19	3	Human	3	2-6	13,2

Table 3: Characteristics of patients with diabetic retinopathy

Parameters	Sex	Age (years)	Diabetes duration (years)	Type of insulin	Number of injections	follow up on (month)	HbA1c (%)
Patient 1	M	14	2	human	<3	irregular	-
Patient 2	M	14	4	human	<3	2-6	10,8
Patient 3	F	19	7	human	<3	irregular	11,8
Patient 4	F	14	6	analog	4	2-6	10,3
Patient 5	M	19	4	human	<3	irregular	7,3

Multivariate analysis of the various parameters studied showed that retinopathy was associated with high HbA1c values (p = 0.043) and poor therapeutic compliance (p = 0.021). As for nephropathy, it was only associated with poor therapeutic adherence with p = 0.0025.

Discussion

The natural history of diabetes is different depending on the means put in place for its management. As one would expect with the difficulties of access to insulin and other accessories for optimal management, our study shows that chronic complications of diabetes are not exceptional in children with T1D. In fact, almost a third of our patients had stunted growth. Knowledge about the management of childhood diabetes is not yet well mastered for both healthcare workers and the general population. Indeed, there are many children who are subject to restrictive diets in the same way as adults with diabetes. This energy restriction has considerable repercussions on the growth of these children. In addition, 65% of our patients were on ordinary insulin, the use of which is more complicated and the results in terms of glycemic balance are worse [3]. In 2018, ISPAD stated that the use of analog insulin associated with a multiple-injection diet contributes to better statural growth by mimicking insulin secretion close to physiology [4]. This contributes to better regulation of the concentration of IGF1 and GH. Elsewhere, authors such as Bekkat Berkani et al, reported a prevalence of stunting at 31.8% and it was correlated with glycemic imbalance and the onset of diabetes during puberty [5]. However, diabetes is probably not the only explanation for this phenomenon. In fact, 40% of our patients come from families with a low socioeconomic level. So probably for these children, they were already in a state of chronic under nutrition long before the discovery of their diabetes. Indeed, stunting is quite frequent in our regions. In Senegal in 2015, UNICEF estimated stunting in the overall pediatric population at 19% [6]. This rather high prevalence is due to the malnutrition, the hemopathies, and the poverty, which prevail in our developing countries. Regarding nephropathy, 20% of screened patients had significant proteinuria. Apart from their age and the poor glycemic balance, no other factor seemed to be associated with the occurrence of this complication. In fact, the patients were all adolescents with an average HbA1c of between 9 and 13%. The other noteworthy fact is the earliness of onset of this nephropathy: ≤ 3 years for 4 of 5 patients. This situation is worrying and should certainly push us to carry out screening earlier while improving the quality of care. In addition, one could ask the question whether there would not be any particularity of diabetes in African children as described in adults. Indeed, studies in adults suggest that Afro-descendants are more likely to develop nephropathy following onset from diabetes than Caucasians [7]. The other particularity in our countries is the use of phytotherapy. In fact, our youngest patient (patient1) used a decoction that had hypoglycaemic properties to the point of being hospitalized several times for severe hypoglycaemia. The product in question has not been identified but the use of these decoctions is strongly associated with renal failure in Senegal. Elsewhere in France, Bouhours-Nouet et al. Reported a similar prevalence of nephropathy in 2005 but with a much larger sample and correlated it with the high figures for glycated hemoglobin [8]. For retinopathy, we were in the same proportions (20%) with 3 patients with macular edema and the other 2 with diffuse microhaemorrhages. However, only one patient (patient4) had both retinopathy and nephropathy, the others had only one or the other vascular complications. We could not explain this, may be a laboratory problem because the assays were not done in the same place. As with nephropathy, the patients were all adolescents with poor glycemic control. In addition to this, they were mainly on regular insulin (4/5 patients) with less than 3 injections per day (4/5 patients) and irregular follow-up (≤1 visit / year). However, it was less early (≥4 years in 4 of 5 patients). Elsewhere, the "Diabcarepediatic" study carried out in Algeria in 2014 reported a single case of retinopathy in 349 children with type 1 diabetes, while in France Barat described 3 cases in 1,500 in France in the same year [9, 10]. However, in other countries, studies had previously shown higher prevalences such as in Finland where the 1993 Falck study of 194 diabetic children reported a prevalence of 10.8%. More recently, another study conducted in England in 2016 by Dhillon et al. reported a prevalence of 19.5%, which is closer to our results. Multivariate analysis of the various parameters studied showed that retinopathy was associated with high HbA1c values (p = 0.043) and poor therapeutic compliance (p = 0.021) [11, 12]. Other authors seem to go in the same direction with other

additional risk factors. Indeed, for Falck but also Ben Mehidi retinopathy in young diabetics in general seems to be linked to the occurrence of diabetes in the pubertal phase, the age of diabetes, non-adherence to therapy and poor balance glycemic. Likewise, Barat correlated it with the increase in the value of glycated hemoglobin, which is also a reflection of a poor glycemic balance. It was the same for Dhillon who correlated with the high figure of glycated hemoglobin and the long duration of evolution. Our study has a certain number of limits, in particular the small sampling but also the nonuniformity of the assays of microalbuminuria [10-13].

Conclusion

Chronic complications of T1D in children are not that rare, especially in our regions where treatment is not optimal. Beyond the recommendations of ISPAD for their screening, we suggest starting it rather around 10-11 years regardless of the duration of progression of diabetes and the means used for management in countries like ours.

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