Scientific Research Publishing

Open Journal of Pediatrics, 2022, 12, 283-292
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Assessment of Insulin Therapy in 281 Children and Adolescents with Type 1 Diabetes in Senegal

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How to cite this paper: Boiro, D., Sow, A., Ndongo, A.A., Basse, I., Thiam, L., Seck, N., Fatoumia, C., Niang, B., Guéye, M., Mbaye, M.N. and Ndiaye, O. (2022) Assessment of Insulin Therapy in 281 Children and Adolescents with Type 1 Diabetes in Senegal. *Open Journal of Pediatrics*, **12**, 283-292.
https://doi.org/10.4236/ojped.2022.121031

Received: January 22, 2022
Accepted: March 28, 2022
Published: March 31, 2022

Abstract

Introduction: In Senegal, with the CDIC "Changing Diabetes In children" project, insulin has been made free. The objective of this study was to evaluate the accessibility and modalities of insulin therapy in the management of type 1 diabetes. **Methodology:** This was a retrospective study including patients followed for type 1 diabetes (T1DM) in hospital between April 2018 and December 2020. **Results:** 281 patients were included. The mean age was 14.22 years. The mean age at diagnosis was 11.28 years. Ketoacidosis was the main mode of discovery of diabetes at 51.6%. Premix and rapid insulins were most commonly used at 84.7% and 82.9% respectively, most often in combination. The most commonly used treatment regimen was three injections/day in 82.5% of cases. The average daily insulin dose was 0.62 IU/Kg/dr. Of the patients, 219 (78%) were self-monitoring of blood glucose. The average number of blood glucose checks was 1.78 per day. 76 patients (27%) went days without an insulin injection and up to 7 days in 51% of cases. The main reasons were forgetfulness, therapeutic errors and stock-outs. Hypoglycaemia was observed in 14.2%. The average glycated haemoglobin was 10%. **Conclusion:** Despite the efforts made, there are still challenges to improve access to insulin. The reinforcement of therapeutic education on insulin therapy is essential for a better quality of life of diabetic children and adolescents.

Keywords

Diabetes, Children, Insulin Therapy, Senegal

1. Introduction

Insulin therapy is the cornerstone of the management of type 1 diabetes (T1DM) and its proper conduct is fundamental for optimal glycaemic control [1]. Contrary to developed countries, access to insulin is still a major problem in our poor countries despite several international efforts. In Senegal, many efforts have been made by the state to make insulin accessible. It is in this perspective, in collaboration with the CDIC project "Changing Diabetes In children", that insulin has been made free of charge as well as several aspects of care throughout the country since 2018 [1] [2]. The objective of this work was to assess the accessibility and modalities of insulin therapy in the management of T1D in order to better identify the difficulties encountered.

2. Methodology

We had conducted a retrospective, descriptive and analytical study including all children and adolescents followed up for T1D, over a period of one year and nine months (from April 2018 to December 2020). Exclusion criteria were patients with incomplete data and diabetics who were not on insulin. The setting of our study was the paediatric department of the Abass Ndao Hospital in Dakar (CHAN). This is a level 3 public health establishment on the Senegalese health pyramid. It is home to the Marc Sankalé Centre, which is the largest centre for the management of diabetes in children and adults.

Sociodemographic, clinical, therapeutic and evolutionary data were collected from the files and recorded on pre-established survey forms. The frequency of diabetes follow-up was monthly, tri-monthly, six-monthly and other. Treatment regimens were defined as one, two, three or four daily injections. Accessibility of insulin was defined by the number of days without insulin. Insulin was accessible if the patient had not had an insulin break in the last 3 months. Glycaemic control was assessed on the basis of glycated haemoglobin (HbA1c) divided into 3 groups: less than 7, 7 to 9, greater than 9. Four HbA1C groups were reported corresponding to four controls at three-month intervals. Patients were classified as lost to follow-up if they had not been seen for more than 6 months from their inclusion date.

The data were entered with Sphinx software version 5.1.0.2. and analysed with SPSS (Statistical package for Social Sciences) version 18. The analytical study was done with cross-tabulations using Pearson's Chi-square test or Fisher's two-tailed exact test according to their conditions of applicability with a significance threshold of $p < 0.05$.

3. Results

3.1. Sociodemographic Data

During the study period, 295 diabetic children and adolescents were followed up, of whom 281 (95.2%) were T1D and under insulin therapy. The average age of the children was 14.22 years with a standard deviation of 3.94 years. Of the patients 79 were over 12 years of age (79%). The sex ratio was 0.6. Most patients lived in suburban areas (56.98%). The number of patients attending school was 201 (71.5%), of whom 71 (41.3%) were behind in their schooling. The socio-economic level was considered low for more than half of the children (54.8%).

3.2. Clinical Data

The majority of the children were pubescent in 48.4% of cases. The majority of the girls (50.3%) had already had their first period. The average age of menarche was 13.8 years with a minimum age of 10 years and a maximum of 19 years (standard deviation was 1.7 years). Regarding family history, the notion of familial diabetes was present in 100 patients (35.6%) and 79 patients (28.1%) had familial parental consanguinity. The mean age of discovery of diabetes was 11.28 years with extremes of 1 and 19 years and a standard deviation of 4.28 years. The patients were older than 7 years in 83.9% (Figure 1). Diabetic ketoacidosis was the finding in 145 patients (51.6%) and cardinal syndrome in 68 patients (24.2%). The patients' body weight was normal in 80% and only 6.7% were overweight.

3.3. Data on Insulin Therapy

The types of insulin used were fast-acting and pre-mixed insulins in 233 patients (82.9%) and 238 patients (84.7%) respectively. Of the patients, 138 (49.1%) injected their own insulin, while parents injected the insulin for 128 (45.2%). Injection was performed with an insulin syringe in 245 patients (87.2%). The mean

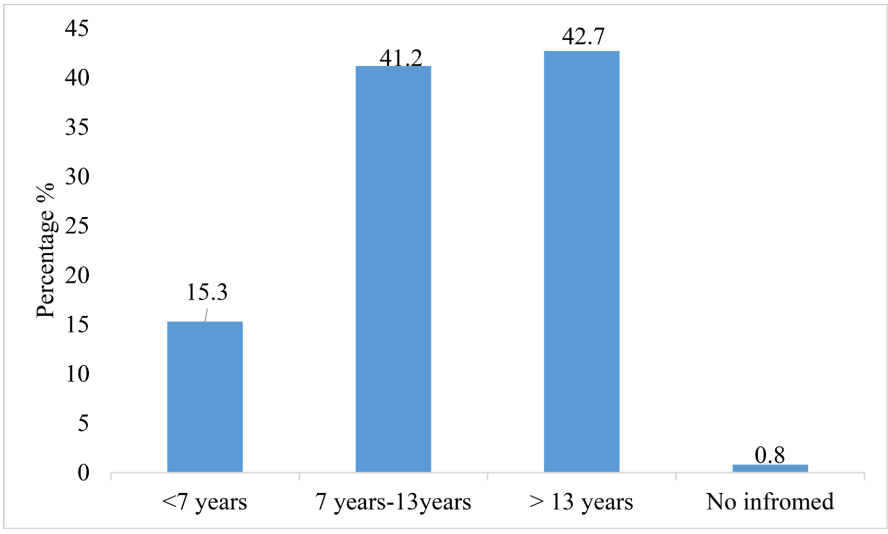

Figure 1. Distribution of patients by age at diagnosis of diabetes.

insulin dose was 0.62 IU/Kg/d with extremes of 0.2 and 2.2 IU/Kg/d. The daily dose of insulin was between 0.5 and 1 IU/Kg in 72.2% of patients compared to 19% who had a daily dose greater than 1 IU/Kg. The 3 injections/day regimen was used in 233 patients (82.9%). All patients had at least one regimen greater than or equal to 2 injections per day. The most commonly used sites were the arms in 226 patients (80.4%), the abdomen in 201 patients (71.5%) and the thighs in 189 patients (67.3%). The injection sites were alternated regularly in 231 patients (82.2%) and daily in 135 patients (48.4%). Of the patients, 76 (27%) remained without insulin injections for days, and a maximum of 7 days in 51% of cases. The main reasons were forgotten injections, therapeutic errors and lack of stock. The data on insulin therapy are summarized in Table 1.

3.4. Data on Follow-Up and Patient Outcomes

The average duration of diabetes was 3.08 years with extremes of 1 and 14 years. Most of the patients had developed diabetes between 1 and 5 years (83.2%). The

Table 1. Summary of data on insulin therapy.

	Parameters	Number	%
Insulin Types	Insulin fast	233	82.9
	Insulin NPH	03	1.1
	Pre-mix	238	84.7
	Fast + NPH	04	1.4
	Slow	00	00
	analogue	36	12.8
Injection methods	Insulin Syringe	245	87.2
	Pen injector	36	2.8
	Insulin Pomp	00	00
Injected Doses	≤0.5 IU/kg/j	24	8.5
	0.5 - 1 IU/kg/j	202	72.2
	>1 IU/kg/j	54	19.3
Treatment regimen	2 injections/day	14	5
	3 injections/day	232	82.6
	4 injections/jour or basal bolus	34	12.1
	No information	1	0.4
Injection sites	Arm	226	80.4
	Abdomen	201	71.5
	Thighs	189	67.3
	Buttocks	81	28.8
	No information	46	16.4

mean glycated haemoglobin (HbA1C) at first check was 10.83% with a minimum of 4% and a maximum of 20.1%. The median was 10.9%. The mean HbA1C at the second check was 10.36% with a range of 4.3 and 16%. The median was around 10.4%. The mean HbA1C at the third check was 10.36% with extremes of 5.3% and 16%. The median was around 10.4%. The mean HbA1C at the last check was 10.75% with extremes of 6.7% and 15%. The median was around 10.5%. (Figure 2)

Of the patients, 216 or 76.8% were hospitalized less than 3 times during their follow-up. The main cause of hospitalisation was ketoacidosis (61.8%) followed by hyperglycemia without ketosis (27.3%). Patients were regularly monitored and attended appointments every three months in 210 cases (74.7%). There were 69 patients lost to follow-up (24.5%) and 2 deaths (0.8%). Of the patients, 219 (78%) were self-monitoring of blood glucose. The average rate of blood glucose monitoring was 1.78 per day, with extremes of 1 and 4. The majority, 163 patients (74.4%), had at least two blood glucose checks per day. Hypoglycaemia was observed in only 40 patients or 14.2%. Lipodystrophy was found in 58 patients (20.6%), mainly in the arms in 28 patients (48.3%) and in the thighs in 18 patients (31%). Seven patients (2.5%) had retinopathy with abnormal fundus, seven (2.5%) had microalbiminuria and two (0.7%) had nephropathy. On the psychosocial level, 9 patients (3.3%) presented a notion of diabetes fatigue and

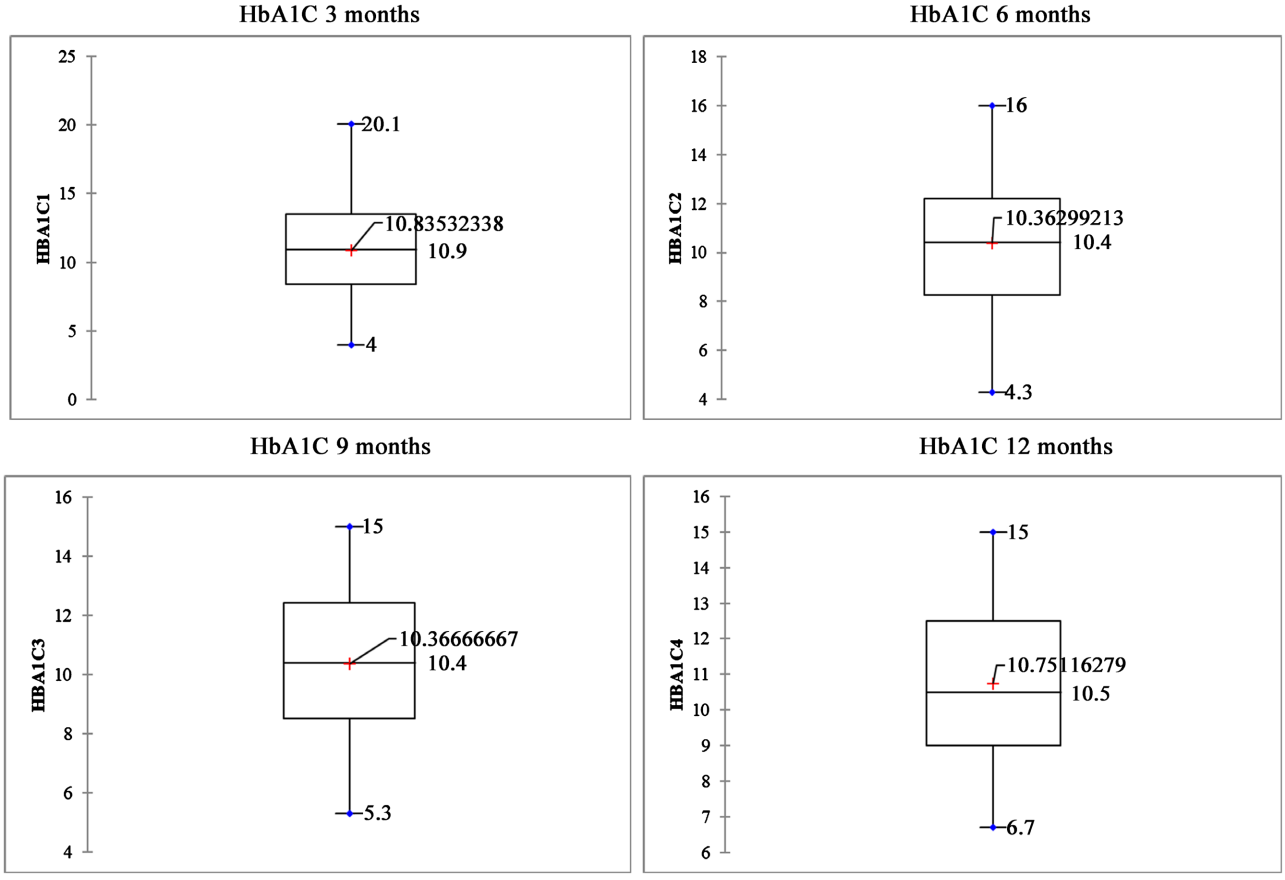

Figure 2. Monitoring of glycated haemoglobin (HbA1C) during follow-up.

six (2.2%) a phobia of injections. The data on follow-up and evolution are summarised in Table 2.

3.5. Analytical Data

Female gender was associated with the occurrence of severe hypoglycaemia. Indeed, girls had more severe hypoglycaemia than boys with a significant p value of 0.018. Severe hypoglycaemia was statistically associated with HbA1C at third check. Half of the patients with an HbA1C < 7% had hypoglycaemia with a p value of 0.045. Statistically, the occurrence of ketoacidosis was not related to the age of the patients. However, ketoacidosis was more common in patients under 5 years of age (71.4%) and in patients between 5 - 11 years of age (57.7%). The occurrence of ketoacidosis was not related to the type of insulin used. However, more ketoacidosis occurred with Rapide + NPH (75%). There was a relationship between the occurrence of ketoacidosis and the daily insulin dose used. There was more ketoacidosis in children taking more than 1 IU/Kg/dr with a p value of 0.045. There was no relationship between the occurrence of ketoacidosis and the treatment regimen. The analytical data are shown in Table 3.

Table 2. Monitoring and progress data.

Data	Parameters	Number	%
Follow-up	Regular	210	74.7
	Not regular	66	23.4
	Lost to follow-up	69	24.5
	Death	02	0.8
	No information	05	1.9
Self-monitoring of blood glucose	1 control/day	55	25.1
	2 controls/day	112	51.1
	3 controls/day	51	23.3
	4 controls/day	1	0.5
Availability of the logbook	Yes	106	37.7
	No	169	60.1
Acute complications	Ketoacidosis	144	73.1
	Hyperglycemia without ketosis	13	6.6
	Hypoglycemia	40	20.3
Chronic complications	Retinopathy	07	2.5
	Nephropathy	02	0.7
	Others	00	00
Psychosocial disorders	Weariness on the diabetes	09	3.3
	Phobia of injections	06	2.2
	Difficulty in adapting to treatment	04	1.4

Table 3. Analytical data.

Data	Parameters	Yes	No	P value
Severe hypoglycaemia and gender	Female	31 (18.2%)	13 (81.8%)	0.018
	Male	9 (8.1%)	102 (91.9%)	
Severe hypoglycaemia and HbA1C	HbA1C ≤ 7%	4 (50%)	4 (50%)	0.045
	HbA1C 7% - 10%	3 (10.7%)	25 (89.3%)	
	HbA1C ≥ 10%	8 (19%)	34 (81%)	
Ketoacidosis and daily insulin dose	≤0.5 IU/kg/day	7 (30.4%)	16 (69.6%)	0.045
	0.5 - 1 IU/kg/day	101 (51.8%)	94 (48.2%)	
	>1 IU/kg/day	32 (61.5%)	20 (38.5%)	
Ketoacidosis and HbA1C 3 months	HbA1C ≤ 7%	1 (12.5%)	7 (87.5%)	0.007
	HbA1C 7% -10%	18 (64.3%)	10 (35.7%)	
	HbA1C ≥ 10%	14 (33.3%)	28 (62.7%)	

4. Discussion

4.1. Incidence, Age and Sex Ratio

Type 1 diabetes is one of the most common chronic diseases in children [3]. In Senegal, a hospital study found a prevalence of 3.6 per thousand in 2015 with 119 cases in 7 years [4]. In our study, 95.2% of T1D cases were found with 281 cases in 2 years, with a spike in 2018 (40.6%). The study population was aged between 1 and 21 years with a mean age of 14.22 years and a predominance of those over 12 years (79%). In addition, they were aged between 3 and 17 years in the study by M. Sarr *et al* in 1990 at the Dakar University Hospital [5] with a mean age of 11.3 years and a predominance of those over 10 years old (75%). The female sex predominated with 171 girls for 110 boys. This differs from hospital studies conducted in Morocco in 2007 [6] which found a male predominance. However, in the literature, there is no real difference in prevalence between the sexes [4].

4.2. Circumstances of Discovery of Diabetes

The diagnosis of diabetes in children and adults is almost always made at the stage of complications, mainly ketoacidosis [7] [8] in our developing countries. This is in contrast to industrialised countries where this complication no longer reveals the disease or has become rare [4] [6]. In our series, 51.6% of patients were diagnosed with ketoacidosis.

4.3 Growth and Pubertal Development

Monitoring of growth and pubertal development in children and adolescents with diabetes is important to assess the effectiveness of treatment. Poor diabetic control may inhibit growth and delay puberty [8]. Most of our patients were

pubertal at TANNER stage IV and V. For girls, more than half (50.3%) had already had their first period. The age of first menstruation was between 10 and 19 years with a mean age of 13.8 years.

4.4. Assessment of Insulin Therapy and Follow-Up

Insulin is vital in T1D [9]. According to the International Society for Pediatric and Adolescent Diabetes (ISPAD), daily insulin needs are 0.6 to 1 IU/Kg/dr in pre-puberty and up to 2 IU/Kg/dr in the pubertal period [2]. In our study, the average dose of insulin was 0.62 IU/Kg/day, which can be compared with several other study cohorts [4] [5] [9]. The aim is to achieve glycaemic control in order to avoid chronic complications while preserving a good quality of life [10]. In our patients, the most commonly used regimen was three injections/day. The four injections/day or basal bolus regimen was used in only 12.1% of cases. The study by B. Niang *et al.* found that a three-injection/day regimen was used in 45.5% of cases, a two-injection/day regimen in 31.8% of cases, and only 6.8% of patients used a basal-bolus regimen [4]. In the Toufiki study in Morocco, the two-injection/day regimen with morning and evening premix insulin was the most commonly used regimen in 72.94% of cases [6]. Premix and rapid insulins were the most used and most often in combination as they were the only free insulins. The most commonly used means of insulin administration in this study was the insulin syringe. Indeed, the syringe is the most widely used means of subcutaneous insulin delivery worldwide [11]. Because of its ease of use, the insulin syringe is the most accessible in terms of cost and therefore most suitable for developing countries. This could explain its wide use among our patients, the majority of whom are of low socio-economic status. Unlike the pen injector, it is a more expensive method of insulin administration and whose availability in some countries remains a problem, although it may improve the convenience and flexibility of treatment [11].

Subcutaneous injection of insulin can be performed in several parts of the body [10]. The injection site is important because it influences the speed and duration of insulin action [6] [12]. In this study, the recommended injection sites were used in our patients. These were mainly the lateral aspects of the arms, the abdomen and the anterior aspects of the thighs. It is recommended to change the injection sites as often as possible in order to prevent the development of lipodystrophy [10] [13].

Poor compliance is frequently observed in our poor countries due to the high cost of insulin [14]. In Senegal, there has been a policy of subsidising insulin to make it more accessible for several years, and in addition to this, in collaboration with the CDIC project "Changing Diabetes In children", insulin has been made free of charge as well as several aspects of management throughout the country since 2018 [1]. In spite of this, we have observed poor therapeutic compliance with insulin skipping in 27% of our patients, often linked to stock shortages. This will cause poor glycaemic control.

The prevention of hypoglycaemia is an important aspect of education for young diabetics on insulin [6]. In our cohort, 14.2% had severe hypoglycaemia. Insulin is injected at specific sites. The injection site is important because it influences the speed and duration of insulin action. In order to avoid the development of lipodystrophy, it is recommended to change the injection site. Although the majority of our patients alternated their injection site, 20.6% had lipodystrophy. Self-monitoring of blood glucose is imperative in young insulin-treated diabetics [10]. In our cohort, the average number of blood glucose checks was 1.78 per day. ISPAD recommends a minimum of 5 self-monitoring of blood glucose per day [15]. This low rate of self-monitoring is also explained by the fact that access to blood glucose monitoring devices is still difficult despite efforts. The American Diabetes Association (ADA) and ISPAD guidelines suggest measuring glycated haemoglobin (HbA1c) at least every 3 to 4 months [6] [7]. The goal is to achieve an HbA1c of less than 7.5% [6]. In this study, four HbA1C values were measured at three-month intervals. The mean HbA1C was around 10% regardless of the order of control. This could be explained by snacking, lack of physical activity and insulin breaks. Psychological support remains essential to improve the acceptance of the disease and the quality of life of the young diabetic patient [14]. In our cohort, psychosocial repercussions were mainly notions of diabetes fatigue and injection phobia. During the follow-up, the majority of patients were regularly monitored and attended to their appointments. However, 24.5% (69) patients were lost to follow-up and 2 (0.8%) died. Rates of loss to follow-up are generally higher in African study, reaching 40% - 45% [4] [9] [14]. In this study, the majority of patients lived in peri-urban areas with low socio-economic levels, making it difficult for them to travel regularly to the city centre where the diabetes reference centres are situated for follow-up.

5. Conclusion

The improvement of access to insulin with the CDIC project remains a fundamental aspect in the prognosis of type 1 diabetes in children and adolescents. Despite the efforts made, there are still some difficulties with this access. In addition, we need to strengthen the therapeutic education of patients and their parents in order to explain to them the modalities of insulin therapy. This will improve the quality of care and achieve better glycaemic control.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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