Metabolic Control in Children with Type 1 Diabetes Mellitus in Sohag University Hospital, Upper Egypt

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Abstract: Background: Prevention of chronic complications of insulin dependent diabetes mellitus (IDDM) in children can be achieved with a good glycemic control. In developing countries, although IDDM represents a serious public health concern, there is little data on etiology and metabolic control in children. **Aim:** To determine the current level of the glycemic control in a sample of children with type 1 diabetes. **Patients and methods:** This prospective observational study was carried out at Pediatric outpatient clinic, Sohag university hospital in the period from 1 July 2009 to 31 December 2011. Children aged 1-12 years with duration of IDDM of more than 1 year were eligible for study. In addition to history, clinical examination (including fundus examination), all included children had there Glycosylated hemoglobin (HbA1C) measured every 4 months for one year. In addition, test for microalbuminuria was done for patients with HbA1C more than 10 %. **Results:** The number of patients that completed the study was 92 patients (56 males and 36 females). Their ages was 7.1 ± 3.1 years. Median duration for IDDM was 16 months. The HbA1C level was 9.0 % ± 2.2 % at the beginning of study and it was 8.9 % ± 1.8 % at the end (P = 0.77). The number of patients with good control (HbA1C < 7.0 %) was only 16 patients (17 %). The number of patients with poor control (HbA1C >10.0 %) was 30 patients (33 %). Poor control was significantly associated with older age (9.2 ± 2 versus 6.3 ± 2.1years, p < 0.001), rural residence (24/42 (57.1 % rural versus 6/50 (12.0 %) urban, p < 0.001, relative risk = 0.25 (95% CI = 0.12-0.52), longer duration of IDDM (22.0 ± 6.8 versus 18.1 ± 7 months, p < 0.02), once daily insulin regimen (12/22 (54.5 %) once regimen versus 18/66 (27.3 %) twice regimen, p < 0.02, relative risk = 0.63 (95% CI = 0.39-1.0). **Conclusion:** Glycemic control in our hospital is poor. This has changed our policy of treatment of IDDM. Shifting treatment of these children from general pediatric outpatient clinic to pediatric diabetes clinic was an essential initial step. Our pediatric diabetes clinic is now being established. An audit to improve glycemic control is underway .

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1.Introduction

Diabetes mellitus (DM) is a common, chronic, metabolic syndrome characterized by hyperglycemia as a cardinal biochemical feature. Type 1 DM is caused by deficiency of insulin secretion due to pancreatic β-cell damage. Type 1 DM is the most common endocrine-metabolic disorder of childhood and adolescence, with important consequences for physical and emotional development. The diabetes control and complications trial (DCCT) showed the importance of strict metabolic control in delaying and preventing complications (1). Recently it is well established that a great percentage of primary and secondary prevention of chronic diabetes complications can be achieved with a good glycemic control — levels of glycosylated hemoglobin (A1C) up to 7% — as much in T1DM (2).

In developing countries (like Egypt) there is little data on etiology and metabolic control in children and adolescents with diabetes (3). The situation in developing countries is further complicated with the fact that: although DM represents a serious public health concern, strict glycemic control is difficult to achieve, owing to financial constraints, cultural obstacles, and lack of adequate infrastructure underlying public services. However, it is known that even in developed countries, the goal of reaching an ideal glycemic control is still a great challenge (4).

Children with poor glycemic control are more likely to have long term complications that further increase medical costs of treatment of diabetes. Therefore studying glycemic control in children with type 1 DM is an integral part of successful management of type 1 DM. Results of these study form the base for further management.

Aim: To determine the current level of the glycemic control in a sample of children with type 1 diabetes.

2. Patients and methods:

This is a prospective observational study carried out at Pediatric outpatient clinic, Sohag university hospital in the period from

Inclusion criteria: 1 July 2009 to 31 December 2011

Age from 1 to 12 years

Duration of diabetes more than 1 year Willing to follow up

Exclusion criteria:

Age less than 1 year or more than 12 years

Newly diagnosed diabetes (less than 1 year duration)

Difficulties in follow up

Ethical approval:

This study was approved by our local ethical committee. Consent was obtained from parents of all children participating in the study

Study protocol:

All included patients have the following done:

- Full clinical history with special emphasis on number of hospital admissions, number of hypoglycemic episodes and number of diabetic ketoacidosis attacks
- Complete clinical examination including anthropometric measurements
- Glycosylated hemoglobin (HbA1C) every 4 months for one year
- Fundus examination
- Microalbuminuria if HbA1C is more than 10 %

Statistical analysis:

Statistical package for social science (SPSS) version 16.0 was used for analysis. Mean and standard deviation were used to express normally distributed data whereas median and range were used to express not-normally distributed data. Student t rest was used to determine the significance of difference between groups in normally distributed data whereas U test was used to determine the significance of difference between groups in not-normally distributed data. We choose significance level of 0.05. Below this level the difference between groups is statistically significant and above which the difference between groups is statistically insignificant

3.Results:

Over the period of study 117 patients were recruited. Out of these 117 patients 25 patients (21 %) did not complete the study and 92 patients (56 males and 36 females) completed the study. Details of these patients are presented in table 1.

Table 1. Demographic data and summary of number of insulin injections of studied patients

Number of patients	92 patients
Age (years)	7.1 ± 3.1 years
Sex	56 males and 36 females
Residence	42 rural and 50 urban
Duration of diabetes	16 months (12 – 38 months)
Number of insulin injections	Twice: 66 patients Once: 22 patients Three times: 2 patients Four times: 2 patients

Fundus examination: This was normal is all studied cases

Number of insulin injections:

Regimen of twice daily premixed insulin injections (70 % intermediate and 30 % rapid acting) was used by 66 children participated in the present study.

Regimen of once daily premixed insulin injections (70 % intermediate and 30 % rapid acting) was used by 22 children participated in the present study.

Regimen of three daily premixed insulin injections (70 % intermediate and 30 % rapid acting) was used by only children participated in the present study.

Regimen of using children morning long-acting insulin and rapid acting insulin injection before the 3 main meals (4 injections/day) was used by only 2 children participated in the present study.

Summary of number of injections was presented in table 1.

HbA1C level:

The number of patients that have their HbA1c measured by their treating physician before the beginning of study was only 12 out of the 92 patients (13 %) participated in the present study. The level was 9.0 % ± 2.2 % at the beginning of study and it was 8.9 % ± 1.8 % ($P = 0.77$).

As there is no significant difference between HbA1C level at the beginning and the end of the study, we will use the HbA1C at the beginning of study for statistical analysis. The number of patients with good control (HbA1C < 7.0 %) was only 16 patients (17 %). The number of patients with poor control (HbA1C >10.0 %) was 30 patients (33 %).

Effect of age on HbA1C:

The HbA1C level was 10.7 % ± 1.3 % in children aged more than 10 years and it was 8.7 % ± 2.3 % in children aged 10 years or less ($P < 0.001$).

Effect of sex on HbA1C:

The HbA1C level was 8.7 % ± 2.5 % in males and it was 9.5 % ± 1.8 % in females ($P < 0.08$).

Effect of number of insulin injections on HbA1C:

The HbA1C level was 8.8 % ± 2.1 % in children with twice injections and it was 9.8 % ± 2.7 % in children with once injection ($P < 0.04$).

Effect of duration of diabetes on HbA1C:

The median duration of diabetes was 16 months (12 – 38 months). There was no correlation between HbA1C level and duration of diabetes (r = 0.12 & P = 0.26)

Effect of residence on HbA1C:

There were 42 rural children and 50 urban children in the present study. The HbA1C level was 9.9 % ± 2.4 % in rural children and it was 8.2 % ± 1.9 % in urban children ($P < 0.001$).

Acute complications:

Hypoglycemia and diabetic ketoacidosis are the most common acute complications of diabetes. We recorded these complications in the studied patients and expressed the results as (number of episodes/1000 children/year) (5). We found that the number of episodes of hypoglycemia was 392/1000children/year and the number of episodes of ketoacidosis was 479/1000children/year.

Associated diseases:

One patient (a female aged 8 years) developed progressive weight loss, pallor, chronic diarrhea and abdominal distension. Her HbA1 C was 7.8 % and she is on twice daily insulin regimen. She has been treated for 2 weeks as an infectious diarrhea without any response. Her blood count showed anemia and her serum calcium was 7.6 mg/dl (normal = 9-11mg/dl). Celiac disease was suspected therefore we did serological tests for celiac disease (tissue transglutamase (TTG) and serum IgA). Her TTG was high and IgA was normal. Small intestinal biopsy showed partial villus atrophy and lymphocytic infiltration. She has been prescribed a gluten-free diet. On follow up there was marked improvement of diarrhea, abdominal distension, pallor and weight gain.

Test for microalbuminuria:

All patients with HbA1C higher than 10 % were investigated for microalbuminuria. Out of 30 patients with HbA1C higher than 10 %, only one patient had microalbuminuria that has been disappeared after 3 months

Analysis of children with poor control:

In the present study there were 30 children (33 % of cases) with poor glycemic control (HbA1C is more than 10 %). Out of these 30 children 18 were males and 12 were females (P = 0.2, Relative risk = 0.67 (95% CI = 0.39-1.3).

Comparison between patients with fair and poor control is presented in table 2. It is clear from this table that older age, long duration of diabetes, once daily insulin injection and rural residence are associated with poor glycemic control

Table2. Comparison between patients with fair and poor control.

	Fair control	Poor control	P value
Number	62	30	< 0.001
Age (year)	6.3 ± 2.1	9.2 ± 2	< 0.001
Duration (month)	18.1 ± 7	22.0 ± 6.8	< 0.02
Number of injections	Twice = 48/66 Once = 10/22	Twice = 18/66 Once = 12/22	< 0.02 Relative risk = 0.63 (95% CI = 0.39-1.0)
Residence	Rural = 18/42 Urban =44/50	Rural = 24/42 Urban = 6/50	< 0.001 Relative risk = 0.25 (95% CI = 0.12-0.52)
Hypoglycemic episodes per 1000 children/year	387	400	< 0.9
Ketoacidosis episodes per 1000 children/year	193	1066	<0.001

4.Discussion

Assessment of glycemic control is very essential initial step in the management and prevention of complications of type 1 diabetes especially in the developing countries like Egypt. The present study was a hospital based study that carried out in Sohag University hospital in Upper Egypt.

In the present study we found that glycemic control in children with type 1 diabetes in our hospital is generally not good. About one third of our patients had poor control and only 17% achieved good glycemic control. The rest of patients had HbA1C value that is relatively high placing the majority of children at a high risk of the complications of diabetes (see results). We also found

that older age, rural residence, less frequent insulin injection (once daily regimen) and longer duration of diabetes were the main predictors of poor control.

Although the mean overall value of HbA1C we observed in the present study is relatively high it is similar to findings of other published studies from all over the world (3, 6, 7). A large population based study was carried out in Scotland (DIABAUD2) recruited 1609 children from 17 centers found that the overall glycemic control was 8.9% (6). National data from Denmark (8) reported mean value of HbA1C of 9.1%. National data from France included 2579 children found that the mean value of HbA1C was 9.0 % (9). However these studies were carried out about 20 years ago. More recently Si et al carried out a research to study and overview diabetes management in five developed countries (Australia, Canada, New Zealand, the US and the UK). They reported that good glycemic control (HbA1C less than 7 %) was achieved in about half of patients (10). Unfortunately good glycemic control was achieved in only 17 % of our patients (see results). Thus concerning glycemic control we are lagging 2 decades behind developed countries. However, our glycemic control is comparable and even better than that of some developing countries (11- 13).

The Diabetes Control and Complications Trial (DCCT) demonstrated that improved blood glucose control over a prolonged period significantly reduces the risk of developing the microvascular complications of type 1 diabetes (1). Although optimizing diabetes care reduces death and complication rates multiple barriers hinder turning evidence into practice especially in developing countries. The overall glycemic control in our patients was 9.0 % (DCCT equivalent 9.1%), which equates to the non intensive arm of the DCCT and is well above the accepted target value. Thus our patients have a high risk of developing complications of diabetes (1, 14). Our explanation for poor control of diabetes in our patients is poor compliance with insulin injections and diet. This also can explain the high rate of acute complications (hypoglycemia and diabetic ketoacidosis) observed in the present study. The present study was carried out in Upper Egypt where low socioeconomic, poor education and poverty are dominant. Therefore, many health problems especially chronic disease as diabetes are very difficult to control owing to financial constraints, cultural obstacles, and lack of adequate infrastructure underlying public services. Moreover, many caring physicians lack the basic knowledge of managing type 1 diabetes as we found that only 13 % of the studied patients had their HbA1c level measured before the start of this study (see results). Many parents found it difficult for them to cope with daily injections, dietry restriction and attending follow up visits (in the present study 25 (21 %) of children did not complete the study).

The most alarming finding in the present study is that one third of the studied children have poor diabetes control (HbA1C higher than 10 %). This put these children at risk of developing many long term complications of diabetes. Furthermore Kim H et al in a large recently published study were able to quantify that: once glycemic control had deteriorated, it is very likely to remain in poor control for extended periods of time (15). Poor glycemic control is a mutifactorial problem as evidenced from many published researches (16- 18). In order to find the risk factors and predictors for poor glycemic control we further analyzed the results of children with poor control (see table 2). We found that older age, longer duration of diabetes, rural residence and less number of insulin injections were the most significant risk factors for poor glycemic control. Our finding that older children are at a high risk of poor glycemic control is in agreement with many studies (19-21). In addition to hormonal changes older children are less compliant with insulin injections and dietry restriction at a time they expected to handle their therapy with less supervision by their parents. This explains the poor glycemic control in older children.

Our finding that long duration of diabetes was a risk factor for poor glycemic control was also observed in published studies (9, 15). Long duration of diabetes especially if associated with poor compliance lead to slow but significant increase in HbA1C and poor glycemic control.

We found that rural children are more likely to have poor glycemic control. In our locality rural residence is further associated with more low socioeconomic status, poor housing and low standards of education. Gallegos-Macias *et al.* found that Lower family socioeconomic status, was associated with a significantly higher HbA1c, regardless of ethnicity (22).

In the present study we found that poor glycemic control was significantly higher in children with less frequency of insulin injections. In treatment of diabetes we aim at giving insulin that is to some extent similar to insulin secretion by pancreas that occur in pouts and peak depending on blood glucose level. Therefore, once daily or even twice daily injections are associated with poor glycemic control (1).

Concerning long term complications, in the present study all children had normal fundus examination and only one patient had microalbuminuria that has been disappeared after 3 months. This to be expected due to short duration of diabetes in our patients (23, 24)

Autoimmune diseases are relatively common in patients with Type 1 diabetes. In the present study one child developed celiac disease (see results). This is in agreement with published studies that were carried out in Egypt (25, 26). The case with celiac disease found in the present study was diagnosed based on clinical features, positive IgA tissue transglutaminase (TTG) and characteristic small intestinal biopsy. The actual number of cases with celiac disease in the present study might be higher if we did screening for all patients. However, we did not perform screening for celiac disease for all patients in the present study. This is in fact one of the important limitations of our study

Implications of this study:

Poor glycemic control in our patients as shown by this study suggested immediate changes in our policy in management of children with diabetes. Shifting treatment of these children from general pediatric outpatient clinic to pediatric diabetes clinic is an essential initial step. Our pediatric diabetes clinic is now being established and all children with diabetes attending our hospital are managed in this clinic. In addition to counseling and dietry advices all children are treated using 4 daily insulin pen injections (long acting insulin once and rapid acting insulin before the 3 main meals). Teaching the parents and their children self monitoring of blood glucose is also integral part of this clinic. We will evaluate our situation in near future by performing regular auditing of the management process.

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