Assessing Factors that Influence the Level of Glycated Hemoglobin in Children and Adolescents with Type 1 Diabetes

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The aim of our study was to assess the factors that influence the level of glycated hemoglobin in children and adolescents with type 1 diabetes (T1D). This study included 122 children and adolescents suffering from T1D who were in the evidence of the First Pediatric Clinic of the Clinical Emergency County Hospital of Craiova between 2003 and 2017. If HbA1c was less than 7.50%, we included patients in the glycemic equilibrium group, and if HbA1c was greater than 7.50%, we considered patients as suffering from unbalanced diabetes. By correlating the glycosylated hemoglobin level with the different parameters used in the study, we observed large/strong positive correlations between HbA1c and duration of diabetes mellitus and also between HbA1c and patient age, HbA1c negative correlation between physical activity, medium/moderate positive correlations between HbA1c and body mass index, weight of the patients and daily insulin dose and the height of the patients included in the study did not show significant correlations. Child and adolescent diabetes management has major adult differences in both insulin and drug treatment, in general, but especially in the need of understanding, counseling and integration specific to these ages.

Key words: type 1 diabetes, glycated hemoglobin, children and adolescents

The type 1 diabetes (T1D) of the child is a chronic disease, evolving in the form of balancing periods, being one of the most common endocrine and metabolic disorders among children and adolescents, caused by the autoimmune destruction of beta cells from the insulin-producing pancreatic islets [1-4].

Worldwide in 2017, according to the International Diabetes Federation, there were about 425 million people with diabetes, and in the year 2045 it is estimated to be 629 million [1]. Moreover, in 2017, besides the 425 million people with diabetes, about 352 million people had impaired glucose tolerance, which places this group of people among those likely to develop diabetes [1-3].

As regards the incidence of this disease among children and adolescents, in 2017 more than one million children and adolescents with type 1 diabetes was exceeded, reaching a prevalence of 1.106 500 cases of type 1 diabetes in the group age 0-19 years [1, 5]. With regard to the total number of new cases diagnosed annually, in 2017, 132 600 children and adolescents with type 1 diabetes were diagnosed [1, 5]. The world's highest rates of diabetes incidence occur in northern Europe [5].

In Romania, according to the ONROCAD study, the risk of developing Type 1 diabetes mellitus is low and remains relatively constant during adolescence, the prevalence of known cases being 3.2% (urban 4 - 4.5% and rural 1.4 – 2.8%) [6]. Recently, the incidence of type 1 diabetes was almost double in all countries, which suggests significant environmental factors in the incidence of this disease.

Although the prevalence of diabetes in children and adolescents is not high, however, the problems caused by this disease, in the most dynamic and at the same time the most critical period of life, are among the most difficult. Children and adolescents have special features and needs and in consequence they need care adapted to their age. Child and adolescent diabetes management has major adult differences in both insulin and treatment in general, but especially in the need of understanding, counseling and integration specific to these ages. Until the discovery of insulin, in 1921, patients with type 1 diabetes died from ketoacidosis coma. After the use of insulin in the treatment of diabetes, an optimistic period of prognosis of this disease followed.

Experimental part

The present study proposed full and detailed evaluation of the factors that influence the level of glycated hemoglobin in children and adolescents with type 1 diabetes.

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Material and methods

The study, a prospective analytical, descriptive observational one, was conducted on a total number of 122 patients diagnosed with T1D, who were selected over a 15 years period (2003-2017). To avoid the bias in this study we included patients consecutively. These patients were diagnosed, recorded and monitored in the First Pediatric Clinic of the Craiova County Emergency Clinical Hospital.

The study was conducted on the basis of a questionnaire which was completed by parents of children and adolescents with T1D, after informed parental consent, in accordance with rules and principles of the Ethics Committee of the University of Medicine and Pharmacy of Craiova and the Ethics Committee of the Clinical Emergency County Hospital of Craiova, approved by these and complied with all the provisions of the international forums regulating the scientific research.

Each parent or legal guardian of the children and adolescents enrolled in the study agreed, by signing the informed consent and acceptance form with the use of clinical and laboratory data from the Medical Observatory Sheet.

Type 1 diabetes was defined according to International Society for Pediatric and Adolescent Diabetes (ISPAD) criteria recognized by international forums: acute onset of insulinopenia symptoms and signs and insulin dependence to prevent ketoacidosis and to survive [7].

We observed the following parameters: the level of glycosylated hemoglobin, origin, age, gender, duration of diabetes, the number of days is physical activity, weight, height, body mass index, insulin dose, the education level of parents the life conditions of the patients, interpretation of blood glucose, the conflicts or other major psychological stressors.

All data was collected and analyzed using the Microsoft Office Excel 2013 software (Microsoft Corporation, Redmond, Washington, USA) where the average and standard deviation for each group was first calculated, then the statistical analysis continued. We used the Student t test to assess the statistical differences between the averages of two data groups, the Z-test for proportions and the Pearson correlation test. In all cases where we had p <0.05 we considered a significant statistical difference.

Results and discussions

This study included 122 children and adolescents known for T1D who were in evidence of the First Pediatric Clinic of the Craiova County Emergency Clinical Hospital between 2003 and 2017. We also published a part of the preliminary results of this study in 2015 [8].

The incidence of this disease increased in the recent years. The severity of this disease is often not recognized, although the complications involved may be very important. This disease affects not only the child, but also the entourage of the child.

Of the 122 children and adolescents, 72 were males (59%) and 50 were females (41%) (fig. 1). The age of



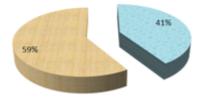
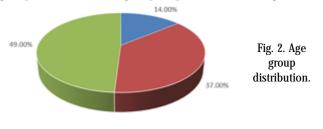


Fig. 1. Gender distribution.

children and adolescents at the time of the study was between 2 and 18 years. The incidence by age group was studied following the inclusion of the 122 children and adolescents in one of the following categories: age group 0 to 7 years, age group 8 to 13 years and age group 14 to 18 years. It was found that 17 patients (14%) were included in the first age group, 45 patients (37%) were in the second group and in the third group 60 patients (49%) (fig. 2).





Taking into account the gender of the patients, we found that 12 male patients (16%) and 5 female patients (10%) were included in the first age group, 26 male patients (37 %), respectively 19 female patients (38%) were included in the second group and the third group included 34 male patients (47%) and 24 female patients (52%) (fig. 3).

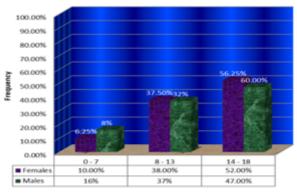


Fig. 3. Distribution of cases by age and gender.

In what the origin of the patients is concerned we noticed that, 66 patients (54.10% of the total patients), including 41 male patients (57% of the total male) and 25 female patients (50% of the total female) were from the urban area, while 56 patients (45.90% of the total patients), including 31 male patients (43% of the total male) and 25 female patients (50% of the total) total female patients (fig. 4) were from the rural area.

Distribution of cases by area of origin and gender

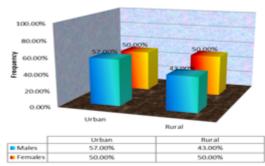
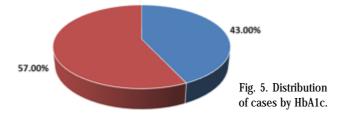


Fig. 4. Rural and urban prevalence.

We then correlated each studied parameter with glycosylated hemoglobin (HbA1c). It should be specified that if HbA1c was less than 7.50% according to ISPAD (8), we included patients in the glycemic equilibrium group, and if HbA1c was greater than 7.50%, we considered patients with unbalanced diabetes. We observed that 52

patients (43% of the total patients) had HbA1c less than 7.51% and 70 patients had HbA1c greater than 7.50% (57% of the total patients) (fig. 5).



HbA1c<7.50% HbA1c >7.50

By correlating the glycosylated hemoglobin level with different parameters used in the study, we observed large/ strong positive correlations between HbA1c and duration of diabetes mellitus (r=0.698, P<0.01, fig.5), but also between HbA1c and patient age (r=0.734, P<0.01, fig.6), HbA1c negative correlation between physical activity (r=-0.595, P<0.01, fig.7), medium/moderate positive correlations between HbA1c and body mass index (r=0.378, P<0.05, fig.8), weight of patients (r=0.418, P<0.05, fig.9) and insulin dose daily (r=0.421, P<0.05, fig.10) and the height of the patients included in the study did not show significant correlations (r=0.146, P>0.05, fig.11).

As we mentioned in the introduction, type 1 diabetes is caused by an autoimmune reaction against the beta cells of the endocrine pancreatic islets, which will cause a decrease in blood insulin levels and an increased glucose level in a chronic way. In the pathogenesis of this disease many environmental factors, genetic susceptibility, but also

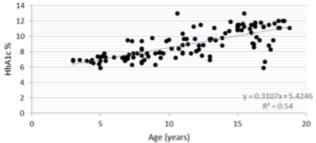


Fig. 6. Correlations between the age of the patients enrolled in the study and HbA1c.

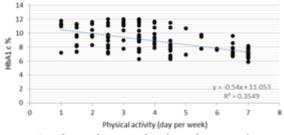
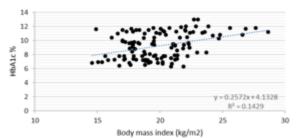


Fig. 7. Correlations between the physical activity of patients enrolled in the study and HbA1c.



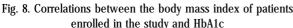


Fig. 9. Correlations between the weight of the patients enrolled in the study and HbA1c.

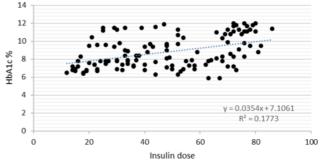


Fig. 10. Correlations between the insulin dose and HbA1c.

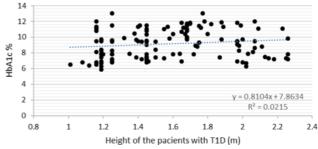


Fig. 11. Correlations between the height of the patients included in the study and HbA1c.

certain viruses, toxins or dietary factors may be involved [9-12].

However, the mechanisms that are fully underlying this disease are not fully elucidated [].

Children with type 1 diabetes should benefit from family support in the first place. But the pediatrician with expertise in diabetes, the diabetes nursing educator, the dietitian, and the mental health expert needs to be involved in managing this disease as well. All these professions should contribute to the proper education of both the children and adolescents with type 1 diabetes and also their caregivers [13-23].

Thus, education must first be provided about how to give insulin, its dosage, and how it works [24, 25]. Also, patients and family should be educated about blood glucose and ketone monitoring, about diabetic ketoacidosis (DKA) prevention, which is among the most common acute complication of diabetes in children and adolescents, while chronic complications are more rarely encountered. There is a need for education in the prevention, recognition and treatment of hypoglycaemia [26-29]. Last but not least, nutritional education and physical activity are very important [30]. As mentioned in our study, the lack of physical activity generally correlates with an increased imbalance in diabetes manifested by elevated levels of glycosylated hemoglobin [31].

Conclusions

As a final conclusion we can say that it is very difficult for children to achieve a metabolic glycemic balance because they pass a difficult period of their lives. A better understanding of the factors that cause glycemic imbalance can significantly contribute to managing this disease and can significantly prevent its complications among children and adolescents.

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