SPECIFIC FORMS OF DIABETES MELLITUS IN CHILDREN AND ADOLESCENTS – THEIR SIGNIFICANCE IN CLINICAL PRACTICE

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Abstract

Although they represent a small group of diabetes mellitus, the specific forms have a burden of difficulties in the field of diagnosis, therapy and prognostic evaluation.

In this study, the authors present their experience in the domain of specific forms of diabetes mellitus, their clinical and biological particularities, their therapeutical approach and evolution.

Diseases with associated diabetes mellitus require compulsory monitoring of glycemia for an early diagnosis and prevention of chronic complications.

Key words: child, adolescent, specific forms of diabetes mellitus

Introduction

Specific forms of Diabetes Mellitus (DM) represent a heterogeneous group of carbohydrate metabolic disturbances in which DM is associated with an isolated or complex morbid clinical picture .[1,2]

The terminology used for this form of disease has undergone lots of changes all through the years. The term "secondary DM" was abandoned; having been considered improper as only in a minority of cases the associated pathology is the actual cause of DM. In majority of cases, DM and associated disease have a common trigger. This is the reason why the term "specific forms' or "form associated with a disease' is preferred to avoid the interpretation of inter-correlated causes. [3,4]

Irrespective of the associated pathology, chronic hyperglycemia retains its specific particularities:

- prolonged subclinical evolution
- early vascular derogatory impact and
- potential to trigger some irreversible, severe vascular or neurological complications. [5,6]

These considerations have justified the present study which proposes evaluation of the proportions of these specific forms of DM, describing their clinical-biological particularities and their evolution modalities.

Material and method

The present study is a retrospective analytic study undertaken on 2198 patients in the records of the IIIrd Pediatric Clinic, Timisoara and the "Cristian Serban" Clinical Center for Evaluation and Recuperation, during the period 1998-2007. The patients presenting chronic disorder of carbohydrate metabolism in the forms of: alterations in fasting glucose, decrease in glucose tolerance and DM type 1 and 2.

In all the patients the fasting glucose ± OGTT, HbA_{1c} were followed in correlation with other metabolic parameters – hormonal or immunological based on the associated carbohydrate metabolism disorder. The average glycemia and the insulin requirement were observed in comparison to patients without associated forms of DM.

Results

Of the 2198 children and adolescents taken in the study, 99 (4.5%) presented specific forms of diabetes (SFDM). (Figure 1).

In terms of the type of carbohydrate metabolism anomaly, 11 (11.11%) patients had altered fasting glucose (AFG), 2 (2.02%) decreased glucose tolerance (DGT) and 86 (86.87 %) had diabetes mellitus. (Figure 2).

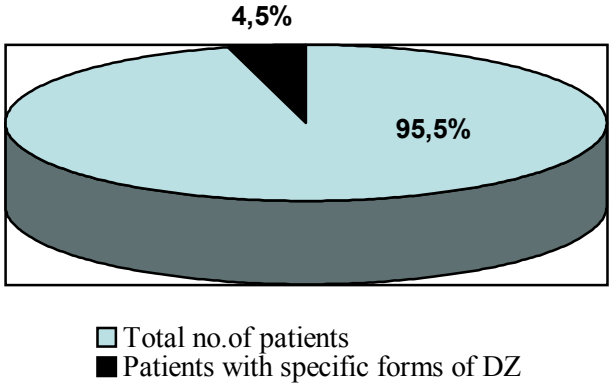

Figure 1. Distribution of patients based on the type of DM.

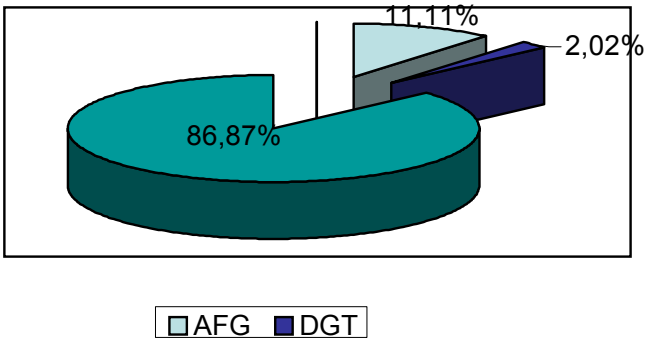

Figure 2. Distribution of patients with SFDM based on the type of carbohydrate metabolism anomaly.

Distribution of patients according to sex in patients without SFDM lot was as follows: 1073 (51.1%) male and 1026 female (48.9%) unlike lot of patients with SFDM in which 30 (30.3%) are boys and 69 (69.7%) are girls. (Figure 3 and Table 1).

Distribution of patients based on age is represented in table 2 and figure 4 and 5.

The specific forms of DM encountered in the studied lot were varied, the main groups being shown in Table 3.

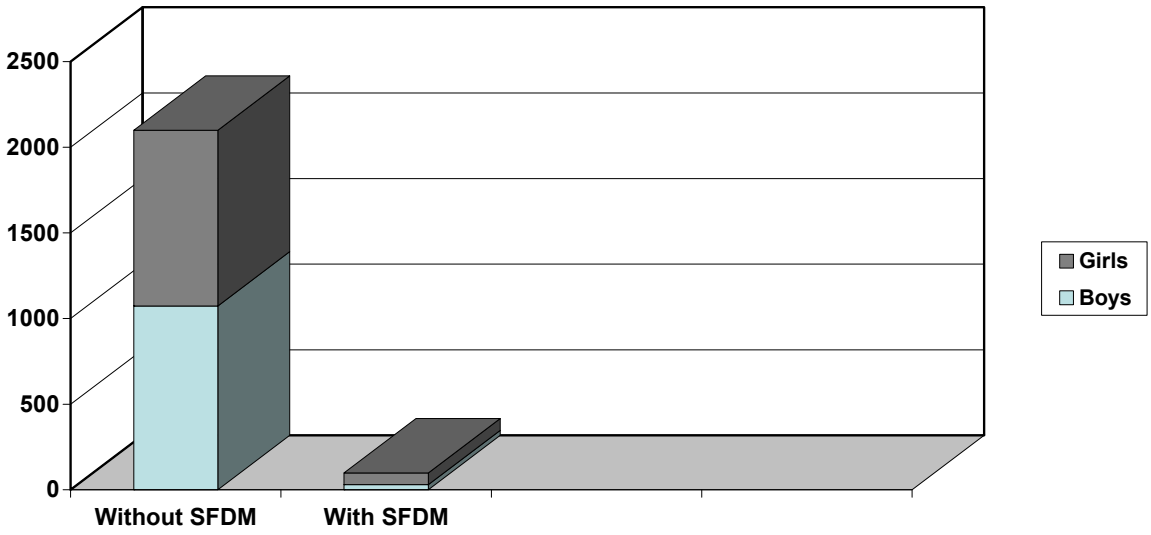

Figure 3. Distribution of patients according to sex.

Table 1. Distribution of patients according to sex.

Sex	Without SFDM	With SFDM	p
Boys	51.1 %	30.3 %	0.052
Girls	48.9%	69.7 %	0.052

Table 2. Distribution of patients based on age.

Age	Patients without SFDM	Patients with SFDM	p
< 3 yrs	1.09 %	2.02 %	0.022
3-6 yrs	5.81%	9.09 %	0.19
7-11 yrs	16.76 %	21.21 %	0.075
12-18 yrs	41.21 %	24.24 %	0.001
19-30 yrs	35.13 %	43.44 %	0.02

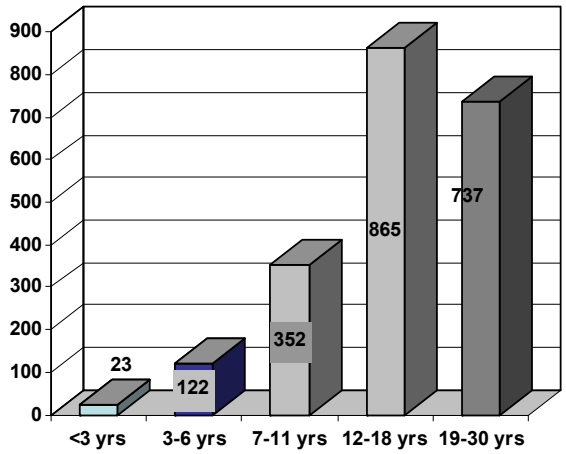

Figure 4. Distribution of patients without SFDM based on age.

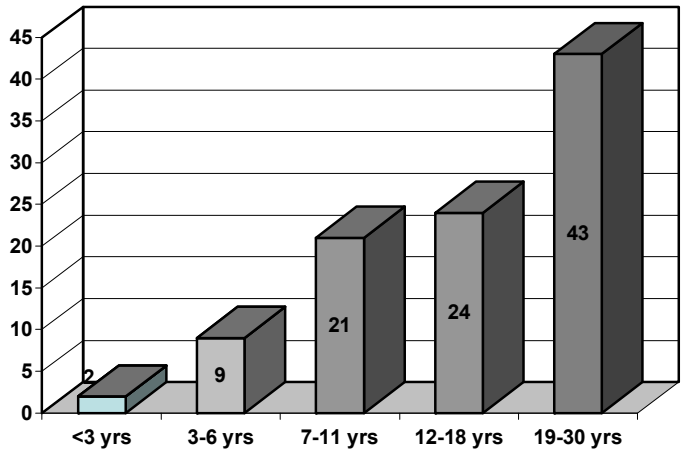

Figure 5. Distribution of patients with SFDM based on age.

Table 3. Specific forms of DM

Specific form of DM	Number of cases	Percent %
Pancreatic diseases	7	7.07
Insulin resistance syndrome (hereditary or acquired)	10	10.10
Genetic diseases	11	11.11
Associated endocrinopathies	34	34.34
Drug induced	25	25.25
Others (congenital and acquired infections, celiac disease, autoimmune disease)	12	12.13

Among the pancreatic diseases which is associated with DM, we encountered in studied lot residual inherited pancreatitis (2 cases), pancreatectomy (1 case), adenocarcinoma (1 case), hemochromatosis secondary to thalassemia (1 case) and cystic fibrosis (2 cases). (Figure 6).

Similarly in the insulin resistance syndrome group, 2 patients had type A (acanthosis nigricans, hyperandrogenism and polycystic ovary syndrome), 5 patients had type B insulin resistance syndrome (acquired by anti-receptor insulin antibodies), 1 case of HIV associated lipodystrophy and 2 patients (brothers) with spastic familial paralysis. (Figure 7).

Genetic diseases associated with DM were dominated by chromosomal disorders and those with genetic obesity:3 cases of Down syndrome and 1 case each of Turner syndrome, Noonan syndrome, Prader-Willi syndrome, Laurence-Moon-Bardet-Biedl syndrome, Kearn Sayre syndrome , Phenylketonuria, Bourneville tuberous sclerosis and albinism. (Figure 8).

Endocrinological pathology dominate this group of patients, being represented by: hypothyroidism - 16 cases, hyperthyroidism - 11 cases, growth hormone deficiency - 1 case, the polycystic ovary syndrome - 3 cases and polyglandular autoimmune syndrome (PGA) type 2 - 3 cases. (Figure 9).

14 patients had corticotherapy induced carbohydrate metabolism anomaly, 3 patients with asparaginase induced and 8 patients by both the drugs. (Figure 10).

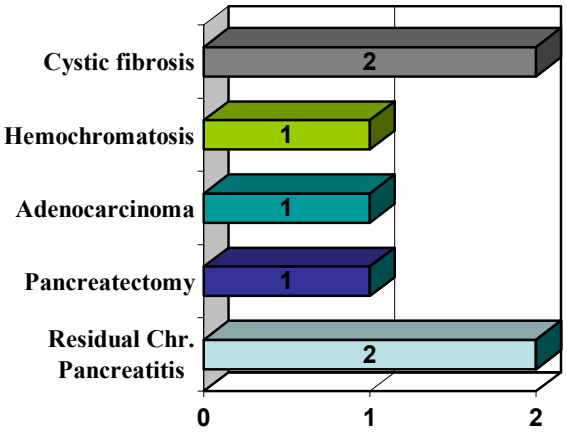

Figure 6. Pancreatic diseases associated with DM.

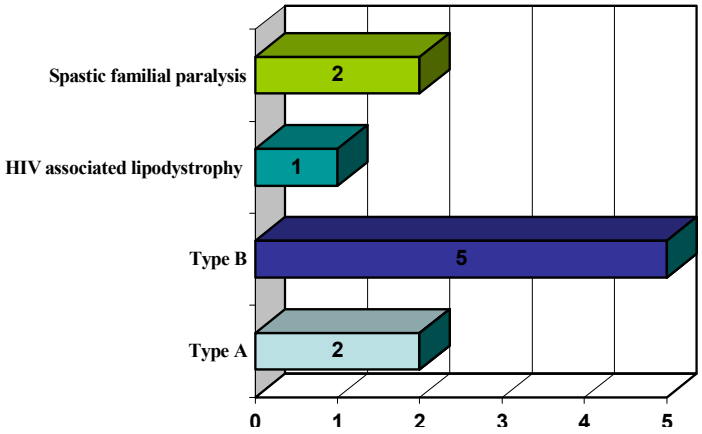

Figure 7. Insulin resistance syndrome associated with DM.

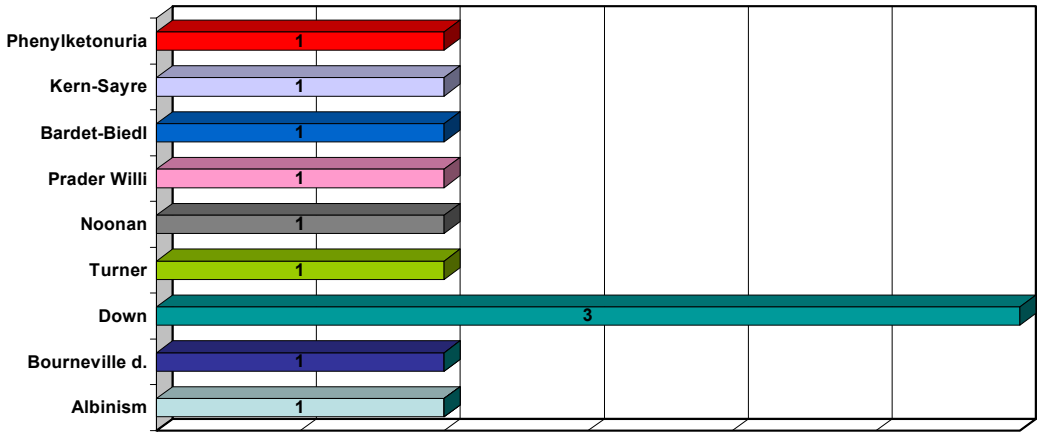

Figure 8. Genetic diseases associated with DM.

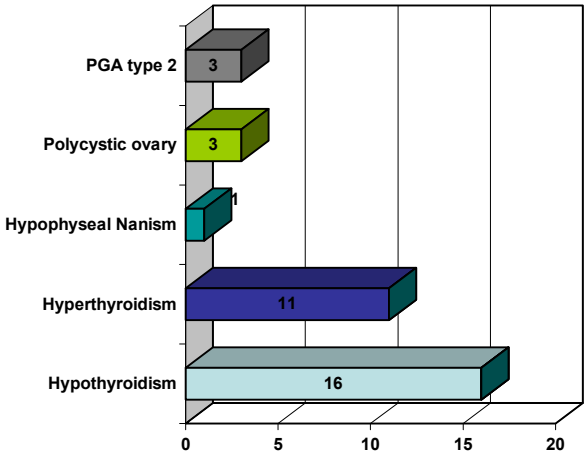

Figure 9. Endocrine diseases associated with DM.

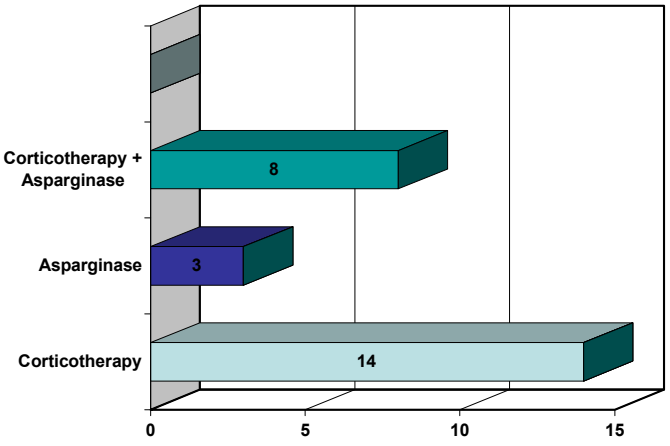

Figure 10. Drug induced DM.

Among congenital and acquired infections that are associated with DM, we observed in the study lot 3 cases of acquired infection with hepatitis C virus and 1 case each of HIV infection, congenital toxoplasmosis, congenital rubella and congenital infection with CMV. (Figure 11).

A specil group was composed of: 2 cases of celiachie, 1 case of spondylitis ankylopoietica, 1 case of Takayasu arteritis and 1 case of chronic glomerulonephritis. A group of autoimmune diseases that are associated with DM is represented in Figure 12.

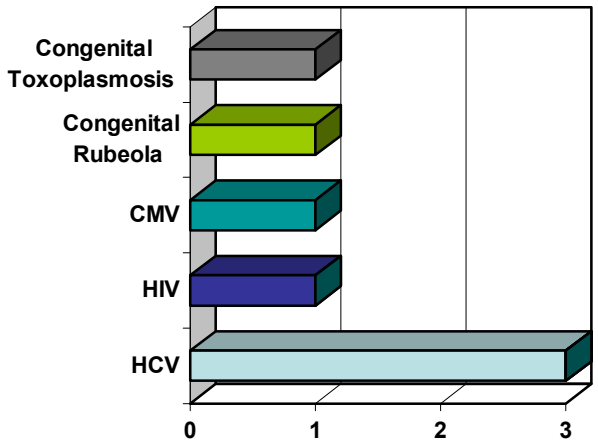

Figure 11. Infections associated with DM.

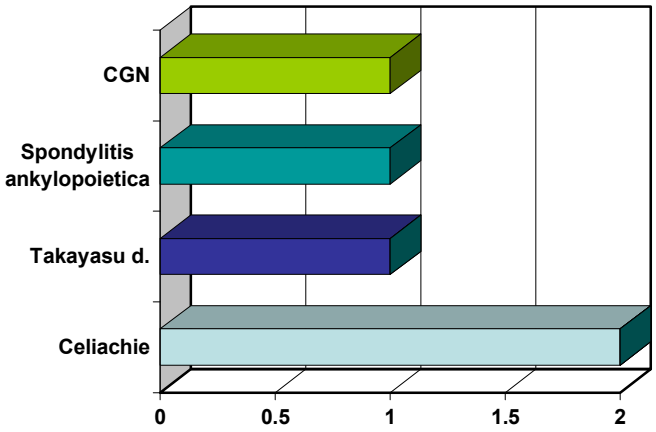

Figure 12. Autoimmune diseases associated cu DM.

Average glycosylated hemoglobin in the lot without SFDM was 9.68% while patients with specific forms of DM had an average HbA1c of 8.29%. (Figure 13 and Table 4).

Insulin requirement was lower in patients with specific forms of DM - 0.6 u/kg/day compared to those without SFDM - 0.87 u/kg/day. (Figure 14 and Table 4).

Table 4. Average Hemoglobin A1c and average insulin requirement.

	Without SFDM	With SFDM	p
HbA1c	9.68 %	8.29 %	0.066
Insulin requirement	0.87 u/kg/day	0.6 u/kg/day	0.022

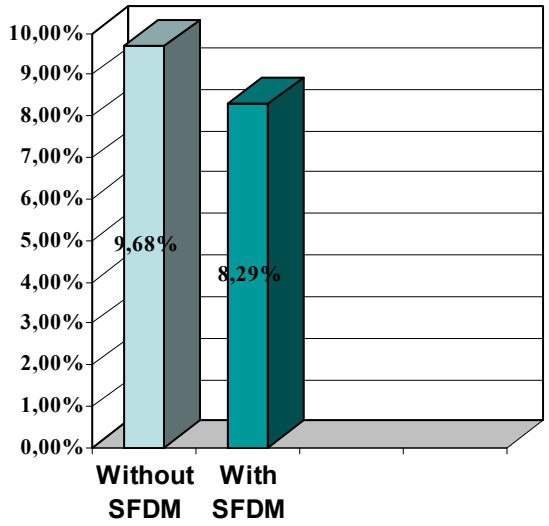

Figure 13. Average Hemoglobin A1c.

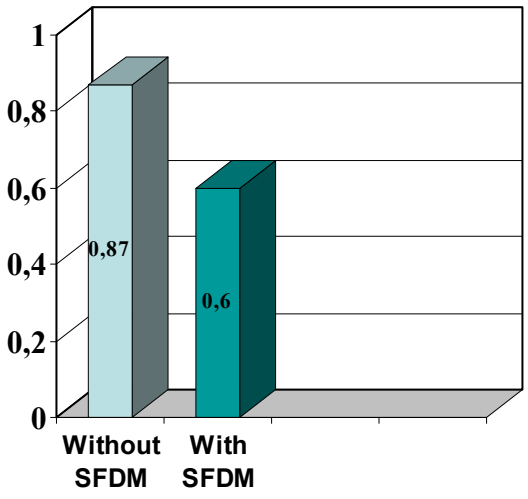

Figure 14. Average insulin requirement (u/kg/day).

Discussions

Chronic hyperglycemia indifferent of the associated pathology has the evolutive risk with regards to the long term complications of vascular or neurological origin. It is well known especially in DM type II but also sometimes in DM type I that complications precede the disease diagnosis. Unhealthy eating habits, smoking, alcoholism, use of anti-contraceptive pills are additional factors that could prompt and worsen these complications.

This is the reason why screening of glycemia disorders has become a compulsory practice, not only for people with high risk (like obesity, DM in siblings, gestational DM, dyslipidemia, polycystic ovarian disease, macrosome newborn etc) but also for the group of patients (though very limited) with diseases known to have an association with DM.

Screening using fasting glucose test, supplemented by OGTT ± HbA_{1c} when required, will ensure an early diagnosis and thus making way to a therapeutical approach for reducing and minimizing the complications.

Specific DM, a relatively small group, making only 4.5% of the total cases of DM in children and adolescents, is a group of diseases with a high degree of discomfort, which needs a complex therapeutical approach as it carries a much higher risk of complications. These morbid associations should be well known and recognized in our clinical practice so as to offer better hope and better quality of life to these patients.

Conclusions

1. Carbohydrate metabolism anomalies associated with other diseases represent 4.5% of the studied lot. Of these, DM represent the majority of cases - 86.7%, while AFG was noted in 11.11% of patients, and DGT in only 2.02% of cases.
2. A predominance of female patients was observed in the SFDM lot.
3. In the SFDM lot, we found almost double the number of patients < 3 years compared to the lot without SFDM, while the proportion was reverse for the 12-18 yr age group.
4. The most frequent SFDM is endocrinopathies, followed by drug induced DM.
5. Average Hemoglobina A1c and average insulin requirements were lower in patients with SFDM.

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