SUMMARY

Type 1 diabetes (DM1 - diabetes mellitus type 1) is one of the most common chronic metabolic diseases of the pediatric population. In the last 30 years, a dynamic increase in the number of cases has been observed, especially in the youngest group, with the rapid onset of the disease that may result in a threat to the child's life. The development of type 1 diabetes, an autoimmune disease, a process resulting from a defect in the immune surveillance system often preceded by the action of non-specific factors (e.g. bacterial and viral infections) and physical or mental trauma (e.g. stress). It is associated with the formation of specific autoantibodies against pancreatic islet antigens and leads to the destruction of insulin-producing beta cells. The presence of antibodies can be detected in the peripheral blood many months or years before the onset of impaired glucose metabolism (pre-symptomatic stage). Therefore it makes it possible to recognize the disease at an early stage. However, only when about 80% of beta cells are destroyed, insufficient insulin concentration leads to severe metabolic disruption that affect the body homeostasis. Currently, in Poland, DM1 in children and adolescents is usually diagnosed at the onset of clinical symptoms, and in about 1/3 of patients life-threatening ketoacidosis is diagnosed, with the need for hospitalization and leads to increased financial outlays for medical care. The development of type 1 diabetes may be also related to the occurrence of the HLA haplotype predisposing to the disease, therefore it is reasonable to take care of the patient's close family members. Detection of the presence of antibodies at the pre-symptomatic stage makes it possible to provide the patient with strict diabetes care, implementation of dietary changes and individual education of the child's family.

Objective of the work:

The main aim of the study was to assess the presence of antibodies against pancreatic islet antigens in children with a positive family history of type 1 diabetes based on selective screening.

Patients with a positive result of the screening test were taken under the care of the Pediatric Diabetes Outpatient Clinic. During the visit to the Clinic, anthropometric measurements were made, the value of glycated hemoglobin (Hba1c) was determined and the oral glucose tolerance test (OGTT) together with the insulin measurements was made after glucose intake of 1.75 g / kg of body weight (max .75g).

Material and methods.

The study involved 268 children aged 9 months to 18 years who had first-degree relatives suffering from type 1 diabetes.

Whole blood samples were collected from the patients (2.7 ml from children under 5 years of age and 5 ml from patients older than 5 years). In order to obtain serum, the collected blood was immediately centrifuged for 10 minutes at room temperature. After centrifugation, the serum was stored in Eppendorf™ tubes, frozen at -20°C. The frozen material was sent to the FIRS Ltd Cardiff center in United Kingdom, where the screening test (ElisaRSR™ 3 Screen ICA™) was performed to determine whether the material contains 1 or more antibodies against pancreatic islet cells: 1/GAD– against glutamic acid decarboxylase, 2/IA-2 – against tyrosine phosphatases, 3/ZnT8 – against the zinc transporter.

In case of a positive test result another detailed test was performed from the same serum sample, including also the presence of antibodies against insulin. The titre of antibodies against ZnT8 ,GAD, IA2 was assessed using ELISA, whereas antibodies againts insulin were assessed by immunoprecipitation.

Obtaining a positive titre of 2 types of antibodies in the blood serum confirmed the positive result of the entire test.

Results:

A total of 268 children aged 9 months to 18 years (mean 8 years) were included in the study. 52.7% of the study group were girls, 47.3% were boys. Of the entire study group, 97% children had one first-degree relative with type 1 diabetes, 2% children had two first-degree relatives with a history of type 1 diabetes, 1% had three relatives with type 1 diabetes. 64% children had siblings with type 1 diabetes, 36% children had affected parents.

Most of the children were at the age of 0-5 years – 89 individuals (38%), 64 children (30%) were at the age of 6-10 years and 72 patients (31%) were 11-18 years old.

Among the whole study group, 24 children (8,9%) were identified with the positive screening test result. Mean age in this group was 8,5 years, 45,5% of them were boys and 54,5% were girls. The highest number of positive test results was observed in the group of 6-10 years old children. 80% of the patients with positive screening test result had a type 1 diabetic sibling, while 20% of them had a parent with DM1.

In patients with a positive screening test result, 71% presented a positive titre of antibodies against GAD, 41.5% - against IA2, 58.5% - against ZnT8, and 25% had a positive titer of IAA antibodies.

Patients identified with a positive test result were then transfered under the care of the Pediatric Diabetes Outpatient Clinic. As a follow-up, an oral glucose tolerance test was performed and glycated hemoglobin was determined. 17 out of 24 patients (74%) with a positive result of the screening test decided to join the follow-up programme. In 62.5% (11 patients) the OGTT result was normal, in 6.25% (1 patient) abnormal fasting glucose was found, and in 31.25% (5 patients) diabetes was diagnosed based on the OGTT. None of the patients developed ketoacidosis.

Conclusions

1. Identification of autoantibodies against pancreatic islet cells in individuals with a positive family history of type 1 diabetes (therefore with a high-risk of the disease) allows early detection of type 1 diabetes (at preclinical stage).
2. Patients provided with an early education and multidisciplinary diabetes care will avoid hospitalization due to a serious condition related to ketoacidosis.
3. In addition, identifying children in the early pre-symptomatic stage of diabetes, with preserved insulin secretion, gives them the opportunity to participate in scientific research aimed at inhibiting the autoimmunity process in the future.