

Original Research

Increasing Incidence of Diabetes Mellitus Type 1 in Children – the Role of Environmental Factors

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Abstract

The incidence of diabetes type 1, a chronic autoimmune disease, may reach the status of an epidemic in the 21st century. The highest incidence of diabetes in the world is observed in Finland. However, in the last 8 years a dynamic rise has been observed in Poland, moving the country toward an intermediate level incidence classification. Environmental factors seem to play a part in the observed increase in diabetes incidence both in Poland and in the world since, by acting on genetically predisposed ground prompt to auto-aggression, they may provoke disease occurrence.

The study was carried out on a group of 511 children aged 0-15 years (255 girls and 256 boys). During the period of analysis (1998-2005) almost a two-fold increase in the diabetes incidence rate was observed (1998-10.4 vs 2005-20.4). The identification of all the factors increasing the risk of diabetes mellitus type 1 shall allow for understanding of diabetes ethiopathogenesis, and thus might create a chance for development of new prevention strategies.

Keywords: environmental factors, incidence, diabetes mellitus type 1, children

Introduction

The incidence of diabetes mellitus (DM) type 1, a chronic autoimmune disease, may reach the status of an epidemic in the 21st century [1]. In accordance with the World Health Organisation report of 2004, for the first time diabetes has outscored an infectious disease, AIDS, as the most important single cause of death in the world, being the first non-infectious disease to gain such primacy (3200 thousands vs. 3000 thousands deaths per year) [1].

The highest incidence of diabetes in the world is observed in Finland (45/100,000 inhabitants/year) [2], and it has increased 4 fold from 1953. Such an increasing ten-

dency remains unremitting. Therefore, it is estimated that in 2020 in Finland it will reach the level of 55/100,000 inhabitants/year [2]. Conversely, the lowest incidence of diabetes is observed in Asia (1-2/100,000 inhabitants/year; 0.1/100,000 in China); in Europe the lowest incidence is reported in Romania (5/100,000 inhabitants/year) [2-3]. Until 1998 the Polish population was classified among those of low incidence of diabetes. However in the last 8 years a dynamic rise has been observed, moving Poland toward an intermediate level incidence classification [4]. Environmental factors seem to play a part in the observed increase in diabetes incidence both in Poland and in the world since, by acting on genetically predisposed ground prompted to auto-aggression, they may trigger the disease occurrence [5-6]. Among environmental factors, the two most analyzed are the influence of viral infections and nutrition patterns in the

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early stages of life [5-8]. Various studies have shown that infection caused by at least three viruses (Mumps virus, Rubella virus and Coxsackie virus B4) may significantly correlate with the occurrence of diabetes type 1 [7]. Numerous diabetologists hold responsible various nutritional factors, including cow milk albumin, eaten during first 9 months of life before intestinal barrier to such proteins has developed [9-10]. Additionally various chemicals, conservatives and preservatives added to nutritional products have been implicated [8, 11-12]. Therefore, it seems interesting and important to carry out an analysis of the DM type 1 incidence in Pomeranian population in the years 1998-2005 and its relation to age and gender of the patients in the context of civilization evolution.

Materials and Methods

The study was carried out on a group of 511 children aged 0-15 years (255 girls and 256 boys) diagnosed with type 1 diabetes mellitus in accordance with the criteria of the American Diabetes Association [13]. A prospective register covering the period from 1st January 1998 till December 31st 2005 for all the newly diagnosed patients of the Department of Paediatrics, Haematology, Oncology and Endocrinology Medical University of Gdańsk was completed. The date of the first insulin injection was decided to be the date of the disease onset. The age of the patient was determined as the number of fully completed years. The group of patients was subdivided in accordance to the age criterion: 0-5, 5-9 and 10-15 years.

The figures characterizing Pomeranian population were quoted after Demographic Annual Reports of the Polish General Statistics Office for the years 1998-2005.

The index of diabetes mellitus type 1 incidence was estimated as a number of new cases per year per 100,000 inhabitants of the Pomeranian region of Poland.

Results

The incidence rate for DM type 1 in children under the age of 15 years in the analyzed years was as follows: in 1998-10.4, 1999-10.5, 2000-12.7, 2001-12.6, 2002-12.8, 2003-15.3, 2004-19.6 and 2005-20.4 (Fig. 1).

The mean incidence rate of diabetes mellitus type 1 for the Pomeranian region was 14.3 during the analyzed 8-year time period.

An in-depth analysis of the obtained data allowed us to observe following correlations:

- during the analyzed period of time (1998-2005) almost a two-fold increase in the diabetes incidence rate was observed (1998-10.4 vs 2005-20.4)
- the observed increase in the incidence rate varied in relation to the patients' age and gender. The highest incidence was noted starting from 2002 in the group of children aged 5-9 (2002-15.0, 2003-19.9, 2004-26.1 and 2005-23.8) and, from 2003 also in the group

0-4 years (2003-7.8, 2004-13.1 and 2005-21.9). On the other hand, in the same period the diabetes incidence rate in the oldest group of patients (10-15 years) remained on a stable level (Fig. 2)

- in the observed period the diabetes incidence rate was higher among girls (mean - 14.8) in comparison with boys (mean-13.8) (Fig. 3).

Discussion

The grounds of such an enormous diversity in the DM type 1 incidence rate observed on different continents and even between neighbouring countries in Europe remains unclear [2-4]. According to several authors, environmental factors seem to play a significant role in the autoimmune processes leading to clinical presentations of signs of DM type 1 in genetically predisposed people [5-10]. Globally, the incidence of diabetes mellitus type 1 increases in the group of children aged 0-16 years [14]. Moreover, it is alarming that in recent years the most dynamic increase is observed in groups of youngest children i.e. 0-4 and 5-9 years [2, 4]. Current results of our studies confirm the reported increase in the diabetes incidence among youngest patients. Our data show that in the Pomeranian region in the last 3 years a greater than 2.5-fold increase in diabetes incidence rate was observed in the group of children aged 0-4, including two cases of newborn diabetes [15]. In Finland, the tendency for fastest growth was also observed in the group of children under 5 years of age [2]. The recently published results of the

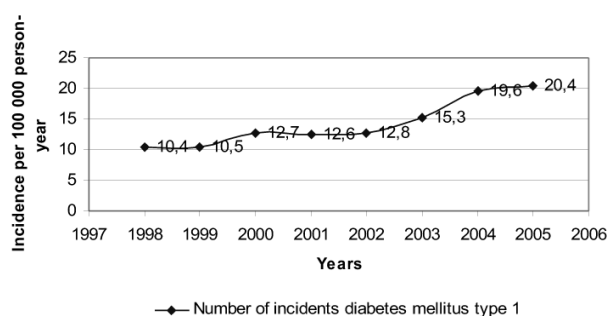


Fig. 1. Incidence rate for DM type 1 children under the age of 15 years in 1998-2005.

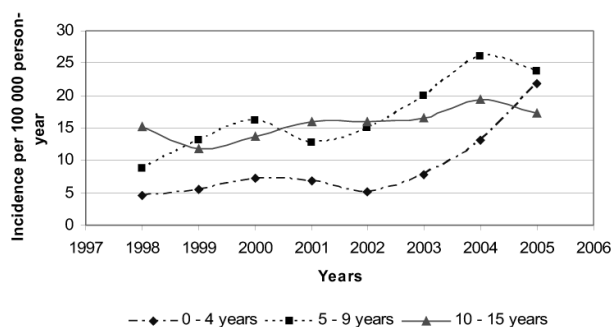


Fig. 2. Incidence rate in the relation with children age.

study from southern Sweden carried out on a group of 21,700 children born between 1997-98 and observed under the ABIS programme showed that male children born in spring, to a mother of low education level, as well as a positive family history for celiac disease, correlated with an increased diabetes incidence rate [5].

Some authors claim that a substantial role in the observed increase in the DM type 1 incidence rate is played by the factors acting in prenatal, perinatal and early-infancy periods [16-17]. In addition to intrauterine infections under consideration as putative risk factors are various supplements to nutritional products (such as: water conditioners, chemicals, conservatives, and preservatives) that are consumed by pregnant women [12, 16-17]. Additionally, early over-feeding, fast growth of an infant in the first 6 months of life, early introduction to the infant diet of cattle proteins, lack or short-lasting natural breast-feeding might be reasons for development of immunologic reaction leading to the destruction of pancreatic β -cells [8-10]. Enteroviral and rotaviral infections that cause gastritis during pregnancy might also be correlated with autoimmunisation of the β -cells in children with genetic predisposition to DM type 1 [18]. Other authors have pointed out the correlation between increased blood interferon- α and the activity of antibodies that indicate past enteroviral infection leading towards autoimmunization [19]. The autoimmunologic process is a long-lasting one, which explains the particularly extended time span between the infection and diabetes mellitus type 1 development observed at times. The patomechanism by which viral infection triggers cellular and humoral cytotoxicity towards pancreatic β -cells is thus far not fully understood. Even just direct destruction of the β -cells might give them the properties of an autoantigen. One of the mechanisms leading to the disease development is the direct damage and destruction of the pancreatic β -cells by the virus [7]. However, in most of cases a diabetogenic influence of the viral infection is of non-direct character, aimed rather at induction of an autoimmune process directed against pancreatic β -cells and therefore leading to their destruction [10,20]. The persistent destruction of the β -cells by active cytotoxic T lymphocytes, NK and K cells, as well as some of the cytokines (IL1, TNF α , IFN γ) probably releases new autoantigens that induce new cellular reactions and for-



Fig. 3. Incidence rate for DM type 1 in girls and boys in 1998-2005.

mation of new antibodies, thus augmenting the process of destruction till their complete decline [19, 21-22].

The intensive search for the factors increasing the risk of diabetes mellitus type 1 development is the subject of numerous research projects around the world. Their identification shall allow for understanding of the DM type 1 etiopathogenesis, and thus might create a chance for development of new prevention strategies.

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References

- SILINK M. Childhood Diabetes: A Global Perspective-Pediatric Diabetes. **6** (suppl. 3), **2005**.
- KARVONEN M, VILK-KAJANDER M, MOLTCHANOVA E, LIBMAN I, LAPORTE R, TUOMILEHTO J. Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. *Diabetes Care*. **23**(10), 1516, **2000**.
- GREEN A, PATTERSON CC. Trends in the incidence of childhood-onset diabetes in Europe 1989-1998. *Diabetologia*. **44** (suppl. 3), B3, **2001**.
- CHOBOT-JAROSZ P, OTTO-BUCZKOWSKA E, KOEHLER B, MATLAKIEWICZ E, GREEN A. Increased trend of Type 1 Diabetes Mellitus in children's population (0-14 years) in Upper Silesia region (Poland). *Med. Sci Monit*. **6**, 573, **2000**.
- WAHLBERG J, FREDRIKSSON J, NIKOLIC E, VAARALA O, LUDVIGSSON J, The ABIS-Study Group. Environmental factors related to the induction of beta-cell autoantibodies in 1-yr-old healthy children. *Pediatric Diabetes*. **6**, 199, **2005**.
- TAYLOR KW. Viruses and diabetes. *Diabet. Med*. **22**, 957, **2005**.
- FILIPPI C, VON HERRATH M. How viral infections affect the autoimmune process leading to type 1 diabetes. *Cell Immunol*. **2**, 125, **2005**.
- VIRTANEN SM, KNIP M. Nutritional risk predictors of beta cell autoimmunity and type 1 diabetes at a young age. *Am J Clin Nutr*. **78** (6), 1053, **2003**.
- LEONARD C, MARGO H, HONEYMAN C. Cow's milk and type 1 diabetes. The real debate is about mucosal immune function. *Diabetes*. **48**, 1501, **1999**.
- PARONEN J, KNIP M, SAVILAHTI E, VIRTANEN SM, ILONEN J, AKERBLOM HK, VAARALA O. Effect of cow's milk exposure and maternal type 1 diabetes on cellular and humoral immunization to dietary insulin in infants at genetic risk for type 1 diabetes. Finnish Trial to Reduce IDDM in the Genetically at Risk Study Group. *Diabetes*. **49**, 1657, **2000**.
- BELLISLE F, DALIX AM, CHAPPUIS AS, ROSSI F, FIQUET P, GAUDIN V, ASSOUN M, SLAMA G. Monoso-

- dium glutamate affects mealtime food selection in diabetic patients. *Appetite*. **26**(3), 267, **1996**.
12. SILINK M. Childhood Diabetes: A Global Perspective. *Hormone Research*. **57** (suppl 1), 1, **2002**.
 13. American Diabetes Association: Diagnosis and Classification of Diabetes. *Diabetes Care*. 20:1183-1197, 1997 and *Diabetes Care*. **26**, 3160, **2003**.
 14. TAPLIN CE, CRAIG ME, LLOYD M, TAYLOR C, CROCK P, SILINK M, HOWARD NJ. The rising incidence of childhood type 1 diabetes in New South Wales, 1990-2002. *Med J Aust*. **183**(5), 243, **2005**.
 15. MYŚLIWIEC M, BALCERSKA A, BAUTEMBACH-MINKOWSKA J, WIERZBA J, MAŁECKI MT, NAZIM J. The usage of the personal insulin pump for treatment of a 7 week infant with neonatal diabetes mellitus. *Endokrynologia, Diabetologia i Choroby Przemiany Materii* (in press).
 16. VISKARI HR, ROIVAINEN M, REUNANEN A, PITKANIEMI J, SADEHARJU K, KOSKELA P, HOVI T, LEINIKKI P, VILJA P, TUOMILEHTO J, HYOTY H. Maternal first-trimester enterovirus infection and future risk of type 1 diabetes in the exposed fetus. *Diabetes*. **51**(8), 2568, **2002**.
 17. STENE LC, HONGVE D, MAGNUS P, RONNINGEN KS, JONER G. Acidic drinking water and risk of childhood-onset type 1 diabetes. *Diabetes Care*. **25**, 1534, **2002**.
 18. SALMINEN K, SADEHARJU K, LONNROT M, VAHASALO P, KUPILA A, KORHONEN S, ILONEN J, SIMELL O, KNIP M, HYOTY H. Enterovirus infections are associated with the induction of beta-cell autoimmunity in a prospective birth cohort study. *J Med Virol*. **69**(1), 91, **2003**.
 19. CHEHADEH W, WEILL J, VANTYGHEM MC, ALM G, LEFEBVRE J, WATTRE P, HOBER D. Increased level of interferon-alpha in blood of patients with insulin-dependent diabetes mellitus: relationship with coxsackievirus B infection. *J Infect Dis*. **181**(6), 1929, **2000**. Epub. 5, **2000**.
 20. ALTING AC, MEIJER RJGM, VAN BERESTEIJN ECH. Incomplete elimination of the ABBOS epitope of bovine serum albumin under stimulated gastrointestinal conditions of infants. *Diabetes Care*. **20**, 875, **1997**.
 21. OBAYASHI H, HASEGAWA G, FUKUI M, KAMIUCHI K, KITAMURA A, et al. Tumor necrosis factor microsatellite polymorphism influences the development of insulin dependency in adult-onset diabetes patients with the DRB1*1502-DQB1*0601 allele and anti-glutamic acid decarboxylase antibodies. *J. Clin. Endocrinol. Metab*. **85**, 3348, **2000**.
 22. MYŚLIWIEC M, BALCERSKA A, ZORENA K, KAMIŃSKA H, NOWACKA M, SIBIŃSKA Ż, WIŚNIEWSKI P, MYŚLIWSKA J. Relationship between level of TNF α , IL6 and risk of renal proximal tubules damage in children with newly diagnosed diabetes mellitus Type 1. *Polish Journal of Environmental Study*. **14**, (Suppl. II, Part I), 292, **2005**.