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Review Article

An overview of the Epidemiology of Type 1 Diabetes Mellitus

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ABSTRACT

Background and aims: T1D is one of the most frequent endocrine and metabolic conditions in children, chiefly occure following an autoimmune demolition. The characteristics of T1D are the autoantibodies detected in the serum of these patients. The present study was performed to briefly explain the genetics, molecular biology and epidemiology of T1D around the world.

Methods: This review was prepared using the databases of Science Direct, Pub-Med, Scopus, Web of Science, reference lists check and hand searching using keywords such as "prevalence", "incidence","aetiology", "clinical manifestation", "T1D" and "risk factors". The selected papers were fully reviewed and required information for the review was extracted and summarized.

Results: One of the interesting topics for researchers is study of genetic and environmental risk factors (such as age, sex, race, genotype, geographic location and season) involved in T1D chiefly occure following an autoimmune demolition of the pancreatic β cells through cell mediated immunity as well as a humoral immune response. Understanding these factors can play a significant role in the clinical care of patients, treatment and prevention of disease. Epidemiological studies around the world show that the incidence of T1D has been increasing. DIAMOND Project, EURODIAB and SEARCH are the most important projects for childhood diabetes. Epidemiological studies around the world demonstrated that the incidence ofT1D has been increasing by 2-5%. Furthermore, in the "US" Sit has been indicated that the prevalence of T1D is approximately 1 in 300 by 18 years of age.

Conclusion: Considering the high prevalence of T1D and related risk factors, strategic planning for disease prevention and reduction is necessary.

Keyword: Type 1 Diabetes; Epidemiology; Childhood Diabetes

INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is a chronic illness characterized by the insufficient production of insulin due to autoimmune destruction of beta cells in the pancreas. However, the disease can develop in adults, onset most often occurs in childhood [1]. T1DM can be considerated as one of the most frequent endocrine and metabolic conditions in children. Information on frequency of childhood onset T1DM are very restricted. As indicated by the International Diabetes Federation (IDF), the number of youth (0-14 years) diagnosed and newly diagnosed cases per year was 497100 and 78900, respectively [2]. In children and teenager, T1D represents80%-90% of diabetes [3]. It was declared that 3 million Americans had T1D in the US in 2010[4]. In the US, the prevalence of T1D in youth more youthful than 20 years was 1.93 /1000 in 2009 (0.35-2.55 in different racial groups) with 2.6%-2.7% relative annual increase but the number of people affected in the world is not known [5]. T1D is chiefly occur following an autoimmune demolition of the pancreatic β cells through cell mediated immunity as well as a humoral immune response. The characteristics of T1D are the autoantibodies detected in the serum of these patients weeks or months prior to the beginning of the disease, but it is not clear that what is the role of these autoantibodies in the pathogenesis of the disease. Some of these autoantibodies are against the islet cell, Insulin (IAA), Glutamic Acid Decarboxylase (GAD, GAD65), protein tyrosine phosphatase (IA2 and IA2 β) and Zinc Transporter Protein (ZnT8A) are the examples of these autoantibodies [6,7]. Several factors have been implicated in the aetiology of T1D include genetic and environmental factors [8]. T1D has a strong relationship with HLA/DR and HLA/ DQ genes. This alleles can be either predisposing or protective [9]. Recent studies showed that viral infections can be expected to result in diabetes [10] include enterovirus, rotavirus, herpes virus, cytomegalovirus, endogenous retrovirus [11,12] and Ljungan virus. Viral factors include congenital rubella [13,14] and other factors such as decreased levels of vitamin D can also be a risk factor for T1D [15,16]. It is interesting that hypothesis as the hygiene hypothesis suggests that in countries where social and economic conditions are very favorable, exposure to contaminants in the ages before the birth and to improve health and living conditions lead to autoimmune diseases is increasing. In addition childhood obesity or rapid growth leading to increased resistance to insulin, the primary feeding infants with cow's milk instead of breast feeding may be involved in causing the disease [17]. However the role of environmental factors in the pathogenesis of this disease is slightly controversial [18]. T1D often starts suddenly and may include symptoms such as the most important polydipsia, polyuria, polyphagia, lack of energy, excessive fatigue, sudden weight loss, slow healing of wounds, frequent infections and blurred vision [2] and diabetic ketoacidosis following severe dehydration especially in children and adolescents. The symptoms are more severe in children than adults. Other autoimmune diseases such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, vitiligo, celiac sprue, autoimmune hepatitis, myasthenia gravis, and pernicious anemia may be seen in patients with T1D [9]. Diabetes Mondiale (DIAMOND) Project [19,20], the Epidemiology and Prevention of Diabetes (EURODIAB) [21] and the SEARCH for Diabetes in Youth (SEARCH) are the most important projects for childhood diabetes will be emphasized [22]. In 1990, the World Health Organization initiated the DIAMOND project with a primary goal to report incidence of T1D in children. In 2000 was reported that 4.5% of children ≤ 14 years of age have diabetes in 50 countries (incidence: 19,164 per75.1 million children) during1990–1994 [20]. After studing of 100 population worldwide, China and South America had lowest incidence (< 1/100,000 per year) and Sardinia, Finland, Sweden, Norway, Portugal, the UK, Canada, and New Zealand) was reported as highest incidence (> 20/100,000 per year).Incidence of diabetes according to the DIAMOND study in the united states including Pennsylvania, Alabama, and Illinois was 10–20/100,000 per year. Incidence between 5-10/100,000 per year was reported in half the population of Europe. In the US, the SEARCH study has been designed to estimate the incidence and prevalence of diabetes in youth less than age 20 years by age, sex, and race/ethnicit [19]. According to the finding of the SEARCH effort approximately, 0.26% of all people within this age group have diabetes [23,24]. During 1989 - 1994, about 28 million children in Europe and Israel were evaluated and the results showed that about 16362 case of them have diabetes. According to DIAMOND report, the standardized annual incidence rate varied from 3.2/100,000 to 40.2/100,000 person years in Macedonia and two regions of Finland, respectively. In some central European countries, annual increase in the incidence rate of

T1D in this period was 3.4% (95% CI 2.5-4.4%) (the rate of increase was noted to be higher)[25].

RISK FACTORS

Several risk factors such as age, sex, race, genotype, geographic location and season have been associated with T1D.

Age

More than 85% of all diabetes cases have been reported in youth < 20 years of age worldwide. Incidence peak of T1D has increased at ages 10-14 years throughout the world. Registries in Europe suggest that recent incident rates of T1D were the highest in the youngest age-group (0-4 years). After puberty, incidence rates decline and appear to stabilize in ages 15-29 years [26].

Gender

Women was affected by most common autoimmune disorders, but in young population with T1D, girls and boys are equally affected [24].

Genotype and genetic risk factors

Among the most important genes can be introduced in susceptibility to T1D is the Human Leukocyte Antigen (HLA) complex on chromosome 6, especially noted for the HLA class II [27]. In fact, about 90% -95% of young people who are diagnosed with T1D have both haplotypes, but about 5 %of people carry this haplotype, will develop disease [28]. Detailed mapping indicates that the polymorphism and the number of Variable of Tandem Repeat (VNTR) is located in the insulin gene promoter, plays a role in T1D susceptibility. Homozygous individuals for shorter repeats as VNTR type I have a high risk for the disease while carriers for longer repeats as VNTR type III protects against T1D. As a result, following the lower induction of insulin and its precursors transcription in the thymus by VNTR type I, tolerance reduce and T1D develop. Conversely, in individuals with VNTR type III variant, insulin-reactive T cells are removed in the thymus by negative selection [1]. Among the other factors considered in T1D, allelic variation in the Interleukin (IL)-2 receptor gene (IL2RA) region[16,29], PTPN22 which encodes the Lymphoid Protein Tyrosine Phosphatase (LYP)[30,31], CTLA-4 which encodes cytotoxic T lymphocyte-associated protein 4 in the IDDM12 region [32] are remarkable.

Seasonality of onset and birth

Several studies evaluated the relationship of diabetes with seasons, although the results have been controversial [33]. In some studies, the prevalence of diabetes have been reported by month of birth and month of diagnosis. McKinney also reported the lowest and the highest rates of T1D in December and April, respectively, in Ukraine [34]. Similar reports have been published also showed that higher and lower rates of T1D among youth people from Europe, New Zealand and Israel born in Spring and autumn, respectively [24]. Such findings was not found in other studies on people from Europe, East Asia and Cuba [35].

TREATMENT & MANAGEMENT

Patients with type 1 diabetes mellitus require lifelong insulin therapy. Most require 2 or more injections of insulin daily, with doses adjusted on the basis of self-monitoring of blood glucose levels. Long-term management requires a multidisciplinary approach that includes physicians, nurses, dietitians, and selected specialists. The American Diabetes Association (ADA) recommends using patient age as one consideration in the establishment of glycemic goals, with targets for preprandial, bedtime/overnight, and hemoglobin A_{1c} (HbA_{1c}) levels. In 2014, the ADA released a position statement on the diagnosis and management of type 1 diabetes in all age groups. The statement includes a new pediatric glycemic control target of HbA1c of less than 7.5% across all pediatric age groups, replacing earlier guidelines that specified different glycemic control targets by age. The adult HbA1c target of less than 7% did not change. Individualized lower or higher targets may be used based on patient need [36].

CONCLUSION

Epidemiological studies around the world show that the incidence of T1D has been increasing by 2-5%. Furthermore, in the US it has been indicated that the prevalence of T1D is approximately 1 in 300 by 18 years of age. One of the interesting topics for researchers is study of genetic and environmental risk factors involved in T1D. Understanding these factors can play a significant role in the clinical care of patients, treatment and prevention of disease. In recent years the idea that T1D is a disease of children and adolescents has changed, so that now the age of onset of symptoms is not considered as an important factor.

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