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Abstract

Type I diabetes constitutes 5%-10% of subjects diagnosed with diabetes and is due to destruction of β cells of the pancreas. Type 1 diabetes accounts for 80%-90% of diabetes in children and adolescents. According to International Diabetes Federation (IDF), the number of youth (0-14 years) diagnosed with type 1 diabetes worldwide in 2013 was 497100 and the number of newly diagnosed cases per year was 78900. These figures do not represent the total number of type 1 diabetes patients because of the high prevalence of type 1 diabetes in adolescence and adults above 14 years of age. One reported estimate of type 1 diabetes in the United States in 2010 was 3 million. The number of youth in the United States younger than 20 years with type 1 diabetes was estimated to be 166984 in the year 2009. The prevalence of type 1 diabetes in the world is not known but in the United States in youth younger than 20 years was 1.93 per 1000 in 2009 (0.35-2.55 in different ethnic groups) with 2.6%-2.7% relative annual increase. Type 1 diabetes is mainly due to an autoimmune destruction of the pancreatic β cells through T-cell mediated inflammatory response (insulitis) as well as a humoral (B cell) response. The presence of autoantibodies against the pancreatic islet cells is the hallmark of type 1 diabetes, even though the role of these antibodies in the pathogenesis of the disease is not clear. These autoantibodies include islet cell auto-antibodies, and autoantibodies to insulin (IAA), glutamic acid decarboxylase (GAD, GAD65), protein tyrosine phosphatase (IA2 and IA2β) and zinc transporter protein (ZnT8A). These pancreatic autoantibodies are characteristics of type 1 diabetes and could be detected in the serum of these patients months or years before the onset of the disease. Autoimmune Type 1 Diabetes has strong HLA associations, with linkage to *DR* and *DQ* genes. HLA-DR/DQ alleles can be either predisposing or protective. This autoimmune type 1 diabetes is characterized by the absence of insulin secretion and is more dominant in children and adolescents.

In addition to the importance of genetic predisposition in type 1 diabetes, several environmental factors have been implicated in the etiology of the disease. Viral factors include congenital rubella, viral infection with enterovirus, rotavirus, herpes virus, cytomegalovirus, endogenous retrovirus and Ljungan virus. Other factors include low vitamin D levels, prenatal exposure to pollutants, improved hygiene and living conditions decreased childhood infections in countries with high socioeconomic status leading to increased autoimmune diseases (hygiene hypothesis), early infant nutrition such as using cow's milk formula instead of breast feeding in addition to insulin resistance in early childhood due to obesity or increased height growth velocity. The role of environmental factors remains controversial. Recent evidence supported the causative effect of viral infections in diabetes.

Type 1 Diabetes often develops suddenly and can produce symptoms such as polydipsia, polyuria, enuresis, lack of energy, extreme tiredness, polyphagia, sudden weight loss, slow-healing wounds, recurrent infections and blurred vision with severe dehydration and diabetic ketoacidosis in children and adolescents. The symptoms are more severe in children compared to adults. These autoimmune type 1 diabetes patients are also prone to other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, vitiligo, celiac sprue, autoimmune hepatitis, myasthenia gravis, and pernicious anemia. The complete dependence on insulin of type 1 diabetes patients may be interrupted by a honeymoon phase which lasts weeks to months or in some cases 2-3 years. In some children, the requirement for insulin therapy may drop to a point where insulin therapy could be withdrawn temporarily without detectable hyperglycemia. A rare form of type 1 diabetes of unknown origin (idiopathic), less severe than autoimmune type 1 diabetes and is not due to autoimmunity has been reported. Most patients with this type are of African or Asian descent and suffer from varying degrees of insulin deficiency and episodic ketoacidosis. This is a distinct form of type 1 diabetes, first described in the year 2000, and has some common features with idiopathic type 1 diabetes being non-immune mediated. It is characterized by ketoacidosis soon after the onset of hyperglycemia, high glucose levels (≥ 288 mg/dl) with undetectable levels of serum C-peptide, and an indicator of endogenous insulin secretion. It has been described mainly in East Asian countries and accounted for approximately 20% of acute-onset type 1 diabetes patients in Japan (5000-7000 cases) with an extremely rapid and almost complete beta-cell destruction resulting in nearly no residual insulin secretion. Both genetic and environmental factors, especially viral infection, have been implicated in the disease. Anti-viral immune response may trigger the destruction of pancreatic beta cells through the accelerated immune reaction with no detectable autoantibodies against pancreatic beta cells. Association of fulminant type 1 diabetes with pregnancy has also been reported.

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