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Diabetes and viral infection

Abstract

Type 1 diabetes (T1D) results from the autoantibody destruction of insulin-producing β-cells in the pancreas, particularly in early childhood. In addition to, immunological and genetic factors, the environmental factors such as viruses are believed to contribute to the type 1 diabete development. Various studies have detected certian viruses in the the pancreas of type 1 diabetic patients and found link between these viruses and T1D development using different techniques. Based on the epidemiological studies the nteroviruses, especially the coxsackievirus B, are the most common viruses found in type 1 diabetic patients. Virus infection might target *β*-cells and induce strong inflammation in the pancreatic *β* –cells, causing the initial step in autoimmunity induction. This review summarize the role of some viruses in the development of type 1 diabetes.

Keywords: type 1 diabetes, virus, autoantibodies, enteroviruses, childhood, epidemiological, *β* –cells, nteroviruses, coxsackievirus B, immunological and genetic factors, virus infections

Volume 6 Issue 2 - 2017

Moahmed Shaheen

Department of Water Pollution Research, Environmental Virology Laboratory, Environmental Research Division, National Research Centre, Egypt

Correspondence: Moahmed Shaheen, Department of Water Pollution Research, Environmental Virology Laboratory, Environmental Research Division, National Research Centre, Egypt, Tel +2 01016710071, Email m_nrc2007@yahoo.com

Received: May 17, 2017 | **Published:** June 30, 2017

Abbreviations: T1D, type 1 diabetes

Introduction

Type 1 diabetes (T1D) is an autoimmune disease characterized by destruction of β cells.[1] Beside genetic factors, environmental factors such as viruses have been reported to be associated with T1D in human. These viruses include Rubella virus and cytomegalo virus,[2,3] coxsackieviruses,[4] mumps virus,[5] Epstein-Barr virus,[6,7] varicella zostar virus,[8] rotavirus,[9] H1N1 influenza virus.[10] Number of viruses has also been shown as causative factors in development of diabetes in animal models.[10–13]

Currently, there are several studies on the relationship between viruses and T1D. It has been found that the enterovirus is one of the most viral infections related to T1D. For example, Honkanen et al.,[14] detected the enteroviral RNA in stool of children who developed autoantibodies with a time lag of several months. Also, there is evidence that this autoimmunity can accelerate T1D in children after infection with enterovirus involving viral RNA in serum.[15] Another epidemiological study from Finland demonstrated that enterovirus RNA was detected more in blood of children with T1D than healthy children.[16] Moreover, extracted data from 24 separate articles found correlation between enterovirus infection and both T1D and type 1 related autoimmune disease.[17]

To study the role enterovirus in T1D development, researchers transfected mice with human islets followed by coxsackievirus B4 (CVB4) infection. Forty seven of Transplanted mice with CVB4 infection developed hyperglycemia with detection of viral RNA in human islet grafts from infected mice.[18] Kime et al.,[19] suggested that CVB5 may trigger T1D via disruption of miRNA-directed suppression of inflammatory cytokines within pancreatic β-cells.

However, some studies have not detected evidence of viral infections before development of T1D. For example, a comparative study was conducted on a large number of children around the world who are type 1 diabetes genetic risk did not find sign of viruses in the children who developed a sudden-onset T1D as compared to children who found negative for autoantibodies.[20] In Norway, a study did not find evidence that enterovirus expected later development of T1D related autoimmunity, however, the virus signs were somewhat more detected at the time of the first test for antibodies positive than in controls.[21]

Older types of viral mump infections are reported to be associated with T1D; however a recent literature review and meta-analysis showed only a weak link between mumps and T1D, with a lot of differences between studies.[5] Another study from Chile suggested the increasing incidence of TID among patients during the pandemic H1N1 influenza between 2009-2010. However, only one case with T1D had confirmed with H1N1 influenza infection.[22]

Several studies reported the link between virus infections and autoimmunity in human. There is now evidence that various infections may increase the risk of developing T1D-associated autoimmunity and autoantibodies. For example, studies have found that in early infancy that exposed to various infections have higher levels of insulin-binding antibodies than babies who autoantibody negative. This observation was find especially significant among babies who exposure to cows' milk formulas before three months of age, suggesting that viruses may interact with cow's milk , inducing this disease.[23–25]

Another study also found that a greater number of diarrheal illnesses resulted from enterovirus and rotavirus were associated with development of islet autoimmunity, but only in children who were exposed to gluten-containing grains either before 4months of age or after 7months of age, when compared with 4-6months of age. The authors also find that there was no link between islet autoimmunity and upper respiratory symptoms, respiratory infections, or fevers.[26] In contrast, there was association between respiratory infections during the early life (first year) of children and islet autoimmunity.[27,28] In Swedish study, the developing islet autoantibodies can be increased in the pregnant woman who infected with enterovirus in early pregnancy.[29]

In contrast, two studies of Finnish and Norwegian children at genetic risk of T1D did not find association between influenza A and Saffold viruses and the development of risk for islet autoimmunity.[30,31] Certain gut microbes (e.g. hepatitis A virus and Helicobacter pylori) are associated with development of lower risk of T1D.[32]

In the opposite direction, some authors reported that the enteroviruses infections can induce protection against autoimmune disease.[33,34] This idea (Hygiene Hypothesis) hypothesis that fewer infections could increase the risk of autoimmune diseases, than people who get recurrent infection in their early childhood. In animal models, fewer infections showed increase in the development of autoimmune disease, while more infections at an early age protected the mice against diabetes (interestingly, infections in some animal models are not necessarily in protection against autoimmune disease).[33] However, Beyerlein et al.,[27] reported that the recurrent infection with respiratory virus in the first year of life were associated with an increased risk of T1D by age 8.

Tracy et al.,[34] suggested that induction or protection of viruses against T1D depends on several factors such as an individual's genetics, the type of virus and its dose, the age of the individual, and whether the individual has previous immunity to that virus. However, one study found the living of children (0-3years but not in later life) in crowded houses was associated with an increased risk factors of developing T1D.[35] In study of all babies born in Southeast Sweden (1997-1999) find a weak link between previous gastrointestinal infections and development of T1D.[36] Virtanen et al.,[37] did not find link between the microbial exposure in the first year of life of children without an indoor dog exposure and T1D, while the exposure of children during early life to an indoor dog reduced odds of developing preclinical T1D.

Conclusion

This article provided data on the role of some viral infections in the development of T1D. Currently, it is well-known that several viruses can initiate/accelerate islet autoimmunity, causing T1D disease. Beside viral vaccination, the ealier diagnosis can manimize the causes, reducing the morbididy and mortality rates in diabetic patients.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

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