

Is Type 1 Diabetes Mellitus Linked to Enterovirus Infections?

Researchers from the Children's Hospital in Westmead, Sydney, Australia have reported that people with type 1 diabetes mellitus (DM-1) are almost ten times more likely than controls to be infected with an enterovirus. Those who had auto-immunity that preceded clinical diabetes also had an increased risk of enterovirus infections.

However, what is unclear is whether the viruses cause the disease or those with auto-immunity or diabetes are simply more vulnerable to infections.

The researchers noted that globally, the incidence of DM-1 has been rising too quickly, especially in children aged less than five years, to be the result of genetic changes alone. Thus, environmental factors have been suspected. To see if they could clarify the issue, the researchers conducted a meta-analysis of studies of enteroviruses and DM-1, and also where molecular viral detection methods were used.

Researchers shortlisted 24 published papers and 2 abstracts which met their study eligibility criteria. Papers which reported more than 1 case cohort had each cohort treated as separate studies, yielding 34 studies. All were case-control studies. The quality of the papers was considered good, but there was a high level of statistical heterogeneity (i.e. the studies were conducted in different ways). 9 studies analysed pre-diabetes auto-immunity (198 cases, 733 controls); 25 analysed clinical diabetes (1,733 cases, 1,784 controls).

It was found that there were significant association between enterovirus infections and diabetes-related auto-immunity (OR 3.7, 95% CI 2.1-6.8),

and also with clinical type 1 diabetes (OR 9.8, 95% CI 5.5-17.4).

However, the researchers noted that the findings did not prove that enteroviruses cause diabetes, but only provided additional evidence that enteroviral infections are associated with DM-1.

The main limitations of the meta-analysis were:

1. the heterogeneity of the studies;
2. that only 10 studies controlled for ≥ 3 known potential confounders; and
3. polymerase chain reactions to detect infections had been performed on samples from various sites which may have different sensitivities to enteroviruses.

The authors also said that larger prospective studies would be needed.

An accompanying editorial stated that the link between enterovirus infections and DM-1 was clear, but the mechanism of the association was not. The association was probably an interplay of viruses, pancreatic beta cells, the innate and adaptive immune systems, and the patient genotype. The association opened the possibility of developing new preventive and therapeutic strategies. **SMA**

Sources

1. Yeung WCG, Rawlinson WD, Craig ME. Enterovirus infection and type 1 diabetes mellitus: systematic review and meta-analysis of observational molecular studies. *BMJ* 2011; 342:d35.

2. Hober D, Sane F. Enteroviruses and type 1 diabetes are clearly linked, but the mechanism is yet to be explained (editorial). *BMJ* 2011; 342:c7072.