Karolinska Institutet

**Institutet för Miljömedicin**

# Autoimmune diabetes in adults

## Epidemiological studies of risk factors and mortality

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i sal Rockefeller, Nobels väg 11, Karolinska Institutet, Stockholm

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## ABSTRACT

Although autoimmune diabetes in adults is a common form of diabetes, knowledge on risk factors and long term consequences of the disease is limited. The aims of this thesis were to investigate the influence of socioeconomic factors (education and occupation), sleep disturbances and psychological well-being on the risk of developing autoimmune diabetes in adults, to investigate whether genetic variation in the melatonin receptor 1B (*MTNR1B*) contributes to the association between poor sleep and type 2 diabetes which has been previously suggested, and finally to investigate the risk of mortality from all causes, cardiovascular disease and ischemic heart disease in adult-onset autoimmune diabetes, with consideration of the possible influence of metabolic risk factors, glycaemic control, lifestyle factors and socioeconomic position.

These studies are based on data from the Norwegian HUNT Study, to date the largest population-based study where incident cases of autoimmune diabetes in adults can be separated from cases of type 2 diabetes. The HUNT Study consists of three separate surveys performed on three occasions in 1984-2008 and contains information from questionnaires, clinical examinations and blood samples. Information on mortality was obtained by linkage to the national Cause of Death Registry. Individuals who were positive for antibodies against glutamic acid decarboxylase and with onset of diabetes at ≥35 years were classified as having autoimmune diabetes in adults.

The main finding of Study I was that high educational levels (university versus primary school) were associated with an increased risk of autoimmune diabetes in adults (HR 1.98, 95% CI 1.21-3.26) after adjustment for BMI, physical activity, smoking, alcohol consumption, and family history of diabetes, whereas type 2 diabetes was more common in those with low education. An increased risk of autoimmune diabetes in adults was also seen in individuals who reported having sleep disturbances and low psychological well-being (HR 1.84, 95% CI 1.10-3.09), a risk similar to that seen in type 2 diabetes (HR 1.31, 95% CI 1.13-1.50) (Study II). The results from Study III indicated that there was no influence of the *MTNR1B* genetic variant on the association between poor sleep and type 2 diabetes. The association remained after adjustment for genotype and was seen in non-carriers as well as in carriers of the risk allele. Mortality from all causes (HR 1.55, 95% CI 1.25-1.92), cardiovascular disease (HR 1.87, 95% CI 1.40-2.48) and ischemic heart disease (HR 2.39, 95% CI 1.57-3.64) was increased in autoimmune diabetes in adults compared to individuals without diabetes. Importantly, mortality risk was as high as in type 2 diabetes, despite a more favourable metabolic risk profile in patients with autoimmune diabetes. In these patients, excess mortality appeared to be primarily associated with poor glycaemic control.

These findings suggest, for the first time, that socioeconomic and psychosocial factors contribute to the development of autoimmune diabetes in adults. The results are in line with previous data indicating that the aetiology of autoimmune diabetes is partly similar to that of type 2 diabetes but suggest, also, that there are other, currently unidentified, environmental risk factors for autoimmune diabetes that remain to be explored. Finally, the results indicate that survival in individuals with autoimmune diabetes with adult onset would be improved by a more effective treatment.


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