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Type 1 Diabetics at high Cardiovascular Risk are better Identified by Advanced Lipoprotein Profile than by Conventional Lipids

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Abstract

Type 1 diabetes is an autoimmune disease characterized by the destruction of insulin-producing beta cells in the pancreas. It primarily affects children and young adults, necessitating lifelong insulin therapy for glycemic control. The pathogenesis involves a complex interplay of genetic, environmental, and immunological factors. Type 1 diabetes presents challenges in managing blood glucose levels, as it requires frequent monitoring, insulin administration, and lifestyle adjustments. Complications associated with uncontrolled diabetes include cardiovascular disease, nephropathy, retinopathy, and neuropathy. Recent advancements, such as continuous glucose monitoring and insulin pump therapy, have improved diabetes management and quality of life for individuals with type 1 diabetes. Additionally, ongoing research focuses on developing immunomodulatory therapies and potential beta cell regeneration strategies. Early diagnosis, individualized treatment plans, education, and psychosocial support are crucial for optimizing outcomes in type 1 diabetes. Multidisciplinary care involving endocrinologists, diabetes educators, dietitians, and mental health professionals plays a vital role in comprehensive management. This abstract aims to provide an overview of type 1 diabetes, its challenges, current management approaches, and emerging therapeutic prospects to improve the lives of individuals living with this chronic condition.

Keywords: Type 1 diabetes; Autoimmune disease; Insulin therapy; Blood glucose control; Complications

Introduction

Type 1 diabetes, also known as insulin-dependent diabetes or juvenile diabetes, is a chronic autoimmune disease characterized by the destruction of insulin-producing beta cells in the pancreas. It primarily affects children and young adults, although it can occur at any age. Type 1 diabetes accounts for approximately 5-10% of all diagnosed cases of diabetes.

Unlike type 2 diabetes, which is often associated with insulin resistance, type 1 diabetes is characterized by an absolute deficiency of insulin. Insulin is a hormone that regulates the uptake and utilization of glucose in the body, helping to maintain normal blood glucose levels [1]. Without sufficient insulin, glucose builds up in the bloodstream, leading to hyperglycemia.

The exact cause of type 1 diabetes is not fully understood, but it is believed to involve a combination of genetic predisposition and environmental triggers. The immune system mistakenly targets and destroys the insulin-producing beta cells in the pancreas, leading to a loss of insulin production. This autoimmune process may be triggered by viral infections, exposure to certain dietary factors, or other environmental factors.

Cardiovascular disease (CVD) is the leading cause of death in people with type 1 diabetes (T1D). People with T1D still present a four- to eight-fold higher risk of cardiovascular disease (CVD) than the general European population, despite a global reduction in the incidence of cardiovascular events, improved glycaemic control, and patient education. In addition, cardiovascular mortality is almost triple that of non-diabetic individuals, even in those with optimal glycaemic control (time-updated HbA1c 6.9% or 51.9 mmol/mol). Although traditional risk factors such as elevated plasma triglycerides, low HDL cholesterol (HDL-C), or high levels of LDL cholesterol (LDL-C) have consistently been linked to cardiovascular disease (CVD) [5,6], these factors do not account for all of the elevated risk that is observed in this population. Also, people with T1D and ideal glycaemic control generally have obviously typical or even "advantageous" traditional lipid profiles (typical or low LDL-C and plasma fatty oils and typical or even raised HDL-C). However, their lipoprotein subclasses appear to have undergone numerous qualitative and functional changes. As a result, the current evidence shifts our focus away from the conventional glucocentric scenario and emphasizes the importance of comprehending and managing other factors that contribute to their high residual cardiovascular risk, such as the lipoprotein disturbances mentioned earlier [2]. There are numerous methods available for identifying these disturbances: ultracentrifugation, angle gel electrophoresis, elite execution fluid chromatography, or atomic attractive reverberation spectroscopy (1H NMR). The latter is more effective because it requires less time to perform, has a higher throughput, and there is less variation between laboratories.

Against this backdrop, we previously investigated the advanced lipoprotein profile and differences between the general population and a cohort of Mediterranean adults with T1D at increased cardiovascular risk using 1H NMR. Our goals in this study are to describe the 1H NMR-assessed lipoprotein profile of our high-risk sample of T1D adults, to look at how it relates to other clinical and laboratory parameters, and to the presence of ultrasound-measured carotid atherosclerosis.

Individuals with type 1 diabetes require lifelong insulin therapy to survive. Insulin is administered through injections or an insulin pump to mimic the normal physiological release of insulin. Blood glucose

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levels need to be monitored regularly, and adjustments in insulin dosage, diet, and physical activity are necessary to achieve optimal glycemic control.

Uncontrolled type 1 diabetes can lead to various complications, including cardiovascular disease, kidney disease (nephropathy), eye damage (retinopathy), nerve damage (neuropathy), and foot problems [3]. However, advancements in diabetes management, including continuous glucose monitoring, insulin pump therapy, and improved insulin formulations, have significantly improved outcomes and quality of life for individuals with type 1 diabetes.

This article aims to provide a comprehensive overview of type 1 diabetes, including its epidemiology, etiology, clinical manifestations, diagnostic criteria, and current management strategies. It will also touch upon emerging research and potential future directions in the treatment of type 1 diabetes, with a focus on improving outcomes and enhancing the lives of individuals living with this chronic condition.

Materials and Method

A retrospective, descriptive case-control study was conducted at Tays, a tertiary hospital in Pirkanmaa, Finland, and used a case-control design. A prospectively collected local endocrinological patient registry included the clinical characteristics, treatment method, and causes of ketoacidosis of all Tays-treated DKA patients under the age of 15 with DKA.

Age at DKA onset, gender, BMI, duration, type of diabetes (DM1, DM2, monogenic, or secondary diabetes), insulin replacement therapy (no insulin, multiple daily injections, or pump therapy), and blood glucose monitoring or self-monitoring were all included in the Endo Registry data. We evaluated patients with DM1 in addition to those with monogenic or secondary diabetes for the statistical analysis [4]. Additionally, the data included the most obvious DKA causes. At the time of the DKA, a specialist evaluated and recorded the causes of the condition using six predefined categories: diabetes that has not been treated with insulin, infection or medication that affects glucose tolerance, device mechanical issues, denatured insulin, and other or unknown causes The following four groups were further subdivided into for implemented insulin therapy: unawareness, learning difficulties, other illnesses, and social factors like alcohol abuse that lead to neglecting insulin therapy or a lack of self-care commitment. The Endo Registry also provided us with the number of DKA episodes that occurred during the time period. Due to a lack of specific data on DKA episodes, patients who moved to another hospital district during this follow-up period were excluded.

By dividing all DKA episodes treated at Tays during the period by person-time, the overall incidence of DKA was calculated. The sum of the time each person was observed was used to calculate person time. Additionally, the annual incidence of DKA in Tays was calculated in relation to the total number of diabetic patients in the Pirkanmaa hospital district. All DKA patients, as well as DM1 and DM2, had their annual incidences separately calculated.

From the pilot version of the Finnish National Diabetes Registry, three controls for each DKA patient were collected. In the event that no control patient could be found in the same municipality, they were taken from the same hospital district [5]. To ensure that there were enough controls, the ages of three patients were changed to +/- 1 year.

Using routinely collected clinical data, laboratory values, other diagnoses, and mortality among patients and controls were gathered from the Finnish National Diabetes Registry for the period. For the patients and a few controls, the index date was the day of the patient's first day of ketoacidosis.

Patients with diabetes were identified using the Finnish version of the 10th revision of the International Classification of Diseases in the pilot version of the Finnish National Diabetes Registry. Since January 2011, diabetes was identified in patients with diagnoses ranging from E10 to E14 who had been registered in the Care Register for Health Care and the Register of Primary Health Care Visits (Avohilmo). The statutory data for all Finnish residents who have been discharged from any Finnish hospital's inpatient care as well as outpatient visits to public health care are collected in these registers, which are kept up by the Finnish Institute of Health and Welfare (THL). During the follow-up period, prevalences of mental and behavioral disorders, such as ICD-10 diagnoses of dementia, alcohol or drug addiction, psychoses, bipolar disorder, intellectual disability, depression, and eating disorders, were gathered. The analyses included both the primary and secondary diagnoses.

For both patients and controls, data on HbA1c (mmol/mol), estimated glomerular filtration rate, low-density lipoprotein cholesterol, urine albumin-creatinine ratio (U-ACR, mg/mmol), and urine albumin were collected less than a year before and less than a year after the index date. Using the CKD-EPI equation, the eGFR was determined. The following three categories of albuminuria were used in the statistical analysis: none, a high level of albuminuria, or a very high level of albuminuria.

Patients with recurring DKA and those with only one episode were compared in terms of their characteristics, treatment options, and DKA causes [6]. In patients with recurring and single DKA, the differences in glycaemic control, comorbidities, and mortality between the patients and their matched controls were examined separately.

Register-based research is exempt from ethical approval and informed consent requirements under Finnish law. This study is thought to be important to public health because it is based solely on registry data and does not involve any contact with the study participants. The study protocol was approved by the National Institutes of Health and Welfare. Throughout the study, the Declaration of Helsinki, good clinical practice, and the new EU regulation on data protection.

Statistical analysis

Statistical software version 17.0, and IBM SPSS Statistics for Windows, version 26.0, were utilized for statistical analyses. Continuous variables were compared between groups using the Student's t-test, Kruskal-Wallis, Mann-Whitney U test, and categorical variables were compared using the 2 or Fisher's exact test. For the matched case-control data, a conditional logistic regression model was utilized [7]. P-values of less than 0.05 were considered to be statistically significant.

Results and Discussion

In this unique situation, it has been proposed the utilization of digestive microbiota modulators, for example, prebiotics and synbiotics, which might work on metabolic and safe capabilities (for example diminished metabolic endotoxaemia, provocative go betweens, further developed lipid digestion and insulin opposition and invigorate the development and movement of valuable microscopic organisms like Lactobacillus spp. Bifidobacterium species A prebiotic is a selectively fermented ingredient that has specific effects on the gastrointestinal microbiota's composition and/or activity and thus benefits the health of the host. Synbiotic is a product that has both prebiotics and probiotics.

Probiotics are live microorganisms that, when given to a healthy person, improve their health.

Some prebiotics and synbiotics have been shown to improve metabolic endotoxaemia and immune function in human studies. Galactooligosaccharides and fructans of the inulin type are the prebiotics that have received the most research, but resistant starch and dextrin, two food compounds, have recently received special attention as prebiotics in clinical trials [8]. However, our search of databases revealed that no systematic review had examined the effects of inulin-type fructans, galactooligosaccharides, and synbiotics on metabolic endotoxaemia and immune function parameters in overweight or obese individuals. To provide a comprehensive summary of the literature regarding the effects of inulin-type fructans, galactooligosaccharides, and related synbiotics on plasma or serum C-reactive protein (CRP), hs-CRP, cytokines, and endotoxin concentrations in adults who are overweight or obese, we conducted a systematic review of randomized controlled trials (RCTs).

Patients with diabetes and superimposed DKA had an average hospitalization rate of 6.3%, and between 2% and 5% of DKA cases resulted in death. It is expected to be extremely uncommon for DKA and ectopic pregnancy to occur simultaneously. A single case study on ectopic pregnancy with superimposed DKA has been documented. The patient had a cardiac arrest while planning the surgery. She was brought to the operating room, where the confirmed ruptured ectopic pregnancy was removed. The patient passed away after four hours.

There are two differences between the current case report and the report [9]. First, despite having elevated blood glucose levels and no diabetes history, occult Type I diabetes is more likely to be present in a 17-year-old than in a 30-year-old. A 17-year-old patient's overlapping DKA and ectopic pregnancy could be explained by this. However, in our case report, it is much less likely that a patient without a diabetes history will develop DKA. Second, the 17-year-old's eventual outcome and recovery from the ectopic pregnancy removal will sadly never be known because she passed away shortly after surgery. In our case, we were able to determine that the patient had normal blood glucose levels following the resolution of the acute insulting event and had a normal hemoglobin A1C without occult diabetes. Patients with hyperglycemia requiring urgent surgery face a significant perioperative risk of morbidity and mortality as a result of this.

Perioperative mortality and morbidity are high for DKA patients. Skin and soft tissue infections, systemic infections, and other perioperative procedures are more common in diabetic patients. Diabetic patients are expected to have a 50% higher risk of perioperative mortality than non-diabetic patients. Diabetes-related long-term complications, such as cardiovascular, neurologic, and ophthalmic complications, which would influence perioperative morbidity, can account for a portion of this estimated risk [10]. However, perioperative complications in hyperglycemic patients without diabetes have been the subject of several studies. Frisch et al.'s study demonstrated that patients with hyperglycemia have significantly increased mortality, complications, and length of stay in the hospital, regardless of diabetes status. One study found that hyperglycemic patients who received insulin prior to surgery had a similar risk of adverse outcomes to those with normal blood glucose, despite the outcomes in hyperglycemic patients.

Conclusion

Although more randomized controlled trials are required to support the clinical use of inulin-type fructans, galactooligosaccharides, or related synbiotics for the treatment of metabolic endotoxemia or low-grade inflammation in overweight or obese individuals, some prebiotics and synbiotics may have an immunomodulatory effect.

The study included 846 control diabetics who did not have DKA from the Finnish National Diabetes Registry and 282 DKA patients treated at Tays. During the course of the study, Tays treated a total of 324 DKA patients. One patient was left out due to non-diabetic ketoacidosis, and 41 patients were left out because they didn't live in the Tays catchment area for the whole time they were followed up.

Cases and matched controls' baseline characteristics are shown. The majority of patients were male, with a mean age of 36 years. 79% of people had type 1 diabetes, 0.4 percent had monogenic diabetes, 6% had secondary diabetes, and 15% had type 2 diabetes.

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Conflict of Interest

None

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