KONOPKA, Agata, SMOŁKA, Weronika, SKRZYPCZYK, Marcin and SMÓŁKA, Leon. Type 1 Diabetes: An In-Depth Review of Pathogenesis with a Focus on the Role of Physical Activity and Dietary Interventions. Quality in Sport. 2024;19:54238. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.19.54238
https://apcz.umk.pl/QS/article/view/54238

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 12.08.2024. Revised: 19.08.2024. Accepted: 29.08.2024. Published: 01.09.2024.

Type 1 Diabetes: An In-Depth Review of Pathogenesis with a Focus on the Role of Physical Activity and Dietary Interventions

Agata Konopka[1,*]; ORCID ID: 0009-0000-1004-0629;
agatakonopka21@gmail.com

Weronika Smołka[2]; ORCID ID: 0009-0001-6352-3840;
s83134@365.sum.edu.pl

Marcin Skrzypczyk[2]; ORCID ID: 0009-0009-9956-7165;
s80532@365.sum.edu.pl

Leon Smółka[2]; ORCID ID: 0009-0004-3793-0372;
s81350@365.sum.edu.pl

1. A. Falkiewicz Specialist Hospital, Warszawska Str 2, 52-114 Wrocław, Poland
2. Medical University of Silesia, Poniatowskiego Str 15, 40-055 Katowice, Poland

* Correspondence: agatakonopka21@gmail.com

Abstract:

Introduction: Diabetes is a chronic disease that significantly impacts the growth, quality of life, and future prospects of affected children. Type 1 diabetes, the most commonly diagnosed form in children, is autoimmune in nature and characterized by inadequate insulin production,

despite initially normal tissue insulin sensitivity. Traditionally, it is viewed as a condition where autoreactive T lymphocytes attack pancreatic β-cells, leading to an increased risk of complications from both high and low blood glucose levels. The disease develops in individuals with a genetic predisposition influenced by environmental factors, and Poland has seen a notable rise in cases, particularly among younger populations. Clinical guidelines stress the importance of diet and physical exercise in managing diabetes. Exercise helps regulate glucose by enhancing glucose utilization and improving insulin action. This review will address the epidemiology, pathogenesis, clinical symptoms, and the preventive benefits of exercise and diet in managing type 1 diabetes.

Purpose of the work: This study aims to review and characterize type 1 diabetes, focusing on the influence of physical activity and dietary interventions.

Materials and methods:
A comprehensive analysis of research papers from PubMed, Google Scholar, Web of Science, Embase, and Scopus was conducted using search terms that included the following keywords: Pompe disease, lysosomal storage disease, myopathy, acid alpha-1,4-glucosidase, glycogen, newborn screening, and enzyme replacement therapy.

Results: The analysis of existing literature indicates that managing Type 1 diabetes effectively requires a multifaceted approach that includes diet and physical activity. A low-carbohydrate diet has shown potential benefits in improving glycemic control, reducing body weight, and lessening insulin requirements, despite a limited number of studies. This dietary approach may also help mitigate the risk of complications associated with the disease. Physical activity, when tailored to individual needs and carefully managed, plays a crucial role in enhancing overall health and glycemic control in Type 1 diabetes patients. However, it is essential to consider and address specific risks such as hypoglycemia and hyperglycemia during exercise to ensure a safe and effective management strategy.

Keywords: type 1 diabetes, pancreatic β-cells, genetic predisposition, physical activity, dietary interventions

Introduction

Diabetes is a chronic disease that profoundly impacts the development, quality of life, and future of affected children. Type 1 diabetes, the most commonly diagnosed form in children, has an autoimmune basis and is characterized by insufficient insulin secretion, despite initially normal tissue insulin sensitivity. It is traditionally viewed as a disease in which pancreatic β-cells are attacked by autoreactive T lymphocytes, putting individuals at risk for complications related to hyperglycemia and hypoglycemia. It is widely accepted that diabetes develops in genetically predisposed individuals influenced by environmental factors. Poland is among the countries experiencing a significant increase in diabetes incidence, particularly in younger age groups [1]. Type 1 diabetes accounts for 5-10% of all diabetes cases and typically presents earlier than type 2 diabetes [2].

Diet and physical exercise are considered the foundation of diabetes management according to all clinical guidelines. These lifestyle modifications are crucial for managing diabetes. Physical exercise aids in glucose regulation by increasing glucose utilization and improving insulin action. Muscle contraction and the resulting increase in blood flow to skeletal muscles lead to glucose uptake through both insulin-dependent and insulin-independent mechanisms. While exercise can lower blood glucose levels, other factors affecting systemic glucose metabolism can influence these effects. To understand the impact of exercise on glucose removal, it is essential to consider the individual components of this process. The translocation of glucose transporter 4 (GLUT4) to the muscle surface is directly stimulated by muscle contraction, which enhances glucose transport into the muscles. Additionally, muscle contraction increases blood flow to the muscles, accelerating glucose dispersion into the interstitial space. Insulin also facilitates the translocation of GLUT4 to the muscle surface. During exercise, glycogen stores in the muscles and exogenous glucose are utilized, creating a glucose/glucose-6-phosphate gradient that promotes further glucose entry into the skeletal muscles. In this review, we will discuss the epidemiology, pathogenesis, clinical symptoms, and the preventive value of exercise and diet in type 1 diabetes [3,4].

Epidemiology

Diabetes is one of the fastest growing global health emergencies of the 21st century. In 2021, 537 million people had diabetes, what is more by 2030, this number will be around 643 million, and in 2024 can even reach 783 million. In Europe in 2021, there were 61 million diabetics, and by 2045, will be 69 million. As we can see, the increase is 13% and it's the lowest one, in North America it's 24% and in Africa it will be 134% [5]. When it comes to the epidemiology of diabetes type 1 in 2021 there were about 8.4 million individuals worldwide, 18% of these cases were younger than 20 years old, 64% were aged 20–59 years and 19% were ≥60 years old. Prediction says that in 2040 an increase in prevalent cases to 13.5-17.4 million. This data proves that T1D is a serious problem for medical services [6].

For the Polish population, latest data are from 2017, when there were 2.53 million people with diabetes and including 157.188 with T1D and 1.55 million with T2D. In comparsion to 2014 when there have been 2.1 million diabetics, 174.547 of them had T1D and 1.1 million had T2D [7].

The increase in number of diabetes type 1 cases is uncanny. What we know is that T1D is the result of a combination of genetic and environmental factors. Genetic factors in this case are certain combinations of HLA genes, especially DR4-DQ8/DR3-DQ-2, known as the highest-risk genotypes and family history of disease. When it comes to environmental factors, there are some triggers which may indicate occurring of T1D in a predisposed person, such as infection and many many antibiotic treatments during the first stages of life, dyslipidemia and obesity. In general, everything that leads to altered microbiota should be considered to be responsible for developing T1D [8,9].

Pathogenesis

Type 1 diabetes results from the apoptosis of pancreatic β-cells. The destruction of these cells in individuals with risk factors usually begins early and often precedes the clinical symptoms of diabetes. T-lymphocyte-mediated insulitis, followed by the presence of one or more types of autoantibodies, indicates the immunological onset of T1D. Individuals with T1D are also more susceptible to other autoimmune diseases, such as Hashimoto's thyroiditis, celiac disease, Addison's disease, vitiligo, and myasthenia gravis. The factors that cause β-cell

destruction are highly diverse and not fully understood. However, genetic and environmental factors are considered to play the main roles. Although the exact triggers for the development of T1D are not yet fully understood, it appears that the disorder is induced by environmental factors in genetically predisposed individuals [10,11,12]. Type 1 diabetes is characterized by a gradual loss of β-cell function over time. As the disease progresses, β-cell function falls below the threshold required to maintain glucose control, necessitating insulin replacement therapy. The development of diabetes can be divided into three stages, with the duration of each stage potentially varying significantly between individuals [13]:

- Stage 1: asymptomatic β-cell autoimmunity, defined by the presence of ≥2 types of autoantibodies, such as GAD65 (GADA), zinc transporter 8 (ZnT8A), insulin (IAA), islet cell antibodies (ICA), and insulinoma-associated proteins (IA-2A and IA-2β), with normoglycemia maintained and no clinical symptoms present.

- Stage 2: asymptomatic β-cell autoimmunity, characterized by the presence of ≥2 types of autoantibodies but with dysglycemia, indicating functional damage to β-cells, and still no diabetes symptoms.

- Stage 3: symptomatic type 1 diabetes, recognized by symptoms of dysglycemia, including polyuria or diabetic ketoacidosis (DKA).

Mechanisms of β-cell destruction and immunological markers

The destruction of β-cells is confirmed by the presence of autoantibodies in the blood, which indicate an autoimmune basis for diabetes. Clinically significant autoantibodies include those against islet cells (ICA), insulin (IAA), glutamic acid decarboxylase (GADA), tyrosine phosphatase (IA2A), and the zinc transporter protein 8 (ZnT8A). Literature indicates that the presence of multiple autoantibodies (≥ 3) is associated with a high risk of developing diabetes, whereas the presence of a single autoantibody related to islet cells generally has low predictive value. Autoantibodies against islet cells (ICA) are detectable in patients with diagnosed type 1 diabetes and in first-degree relatives of these patients, often months or years before clinical symptoms appear [14,15].

The immune system plays a crucial role in β-cell function and survival, as well as in generating signals that impact the immune system. For example, exposure of β-cells to cytokines in the islet environment at various stages of insulitis—such as type I interferons (mainly IFNα) during the early stages of inflammation, followed by IFNγ, IL-1β, tumor necrosis factor (TNF), and potentially IL-17 at later stages—leads to stress, changes in alternative splicing, and increased expression of HLA class I. These effects, combined with increased chemokine production by β-cells and enhanced cell death, may result in intensified presentation of β-cell neoantigens to immune cells, potentially exacerbating or amplifying the immune attack. β-cell destruction is primarily associated with elements of cell-mediated immunity, such as macrophages, various subpopulations of T lymphocytes, and inflammatory response mediators (cytokines, free radicals). It has been shown that Th1 lymphocytes accelerate autoimmune diseases, including type 1 diabetes, while Th2 lymphocytes inhibit these processes, thus playing a protective role [16,17].

The presence of islet-specific autoreactive CD4+ and CD8+ T lymphocytes in peripheral blood, pancreatic draining lymph nodes, and insulitis lesions provides evidence that type 1 diabetes (T1D) is an autoimmune disease. In this condition, disturbances in thymic education are responsible for the immune system's attack on its own insulin-producing cell

proteins. Regulatory T cells (Tregs), which are crucial for suppressing these autoreactive T lymphocytes in healthy individuals, show a similar frequency in both control individuals and patients with T1DM, but with reduced suppressive capacity in T1DM patients. Interestingly, autoreactive T lymphocytes exhibit atypical characteristics compared to T lymphocytes that protect against cancers and infections, such as relatively low epitope binding affinity for HLA and low T cell receptor (TCR) avidity for HLA-epitope complexes [18].

Genetic Predisposition

In the 1980s, Eisenbarth proposed the current model for the development of the immunological form of type 1 diabetes. While our understanding has significantly advanced since then, the fundamental aspects of this model remain relevant. This model posits that every individual has some degree of susceptibility to developing type 1 diabetes, with susceptibility varying from high in some individuals to very low in others. This susceptibility is largely hereditary, primarily associated with HLA DR and DQ genotypes, and to a lesser extent with many other genetic loci known as IDDM (insulin-dependent diabetes mellitus) susceptibility genes [2].

Genetic studies have revealed that the hereditary predisposition to type 1 diabetes is polygenic. The risk of developing T1DM is largely determined by HLA class II genes, with HLA alleles likely accounting for about 40–50% of the genetic risk. The HLA class II gene region has a complex structure, comprising three loci: DR, DQ, and DP, each containing a variable number of α and β chain genes. Among these, HLA-DRB is the most polymorphic locus and consists of the HLA-DRB1 gene. It can also include additional genes such as DRB3, HLA-DRB4, HLA-DRB5 and pseudogenes HLA-DRB2, HLA-DRB6, HLA-DRB7, HLA-DRB8 and HLA-DRB9, depending on the haplotypes of 13 genes. In clinical practice, the most significant genes are DRB1, with over 400 allelic variants, DQA1, with 25 allelic variants and DQB1, with 57 allelic variants. Significant population differences exist in the frequency and spectrum of HLA haplotypes, both among populations globally and within different regions of Europe [11,19,20].

Historically, genetic risk was assessed based on family history, HLA typing, and genotyping of other loci associated with type 1 diabetes. Recently, summarizing genetic risk using genetic risk scores (GRS) and polygenic risk scores (PRS) has proven to be an effective method for measuring inherited risk. It is important that all predictors included in these models have high prognostic value. However, due to limited knowledge about the contribution of some rare genetic variants of T1D risk, predictive models currently consider only gene variants strongly associated with mechanisms of islet autoimmunity and related dysregulation of antigen-presenting cells, T cell signaling activation, and regulation of T1 interferon levels and cytokine signaling. These models are continually refined with new genetic and epigenetic data [20,21].

The genetic relationship between type 1 diabetes (T1D) and type 2 diabetes (T2D) is particularly interesting, as loci associated with these diseases were previously considered almost entirely distinct, despite some phenotypic overlap. However, recent research has identified several shared risk genes or genetic polymorphisms. Some of these shared risk genes interact with each other, regulating important pancreatic islet functions that are disrupted by disease-associated variants, leading to β-cell dysfunction [10]. Although the genetic predisposition to type 1 diabetes (T1D) is not fully defined, it is evident: the concordance rate among identical twins is 60%–70% with long-term follow-up, and first-

degree relatives have a 5%–6% risk of developing T1D over their lifetime. Despite this clear genetic risk, most individuals with T1D do not have a family history of the disease [22].

Environmental Risk Factors

Environmental factors can modify the response to self-antigens. While these factors are likely not necessary to initiate the autoaggression process, they can, through various mechanisms, render β-cells more susceptible to apoptosis and necrosis. Prospective birth cohort studies have facilitated the identification of potential triggers of islet autoimmunity (IA) and the natural history of progression to T1D [13]. It is widely accepted that factors potentially initiating β-cell-directed autoimmunity include viral infections (e.g., Coxsackie, rubella, enteroviruses, rotaviruses, cytomegalovirus), gut microbiota composition, diet, metabolic stress, inflammation, pollutants, and toxins. The combination of these environmental factors with genetic predisposition and specific epigenetic modifications initiates the autoimmune destruction of pancreatic β-cells [11,13,22].

Beta cells are susceptible to viral infections due to their production of specific receptors and adhesion molecules. The Coxsackievirus and adenovirus receptor (CAR), which is unique to beta cells and located in insulin-containing granules, can increase the vulnerability of these cells to viral infections during insulin secretion. Studies correlating enteroviral infections with islet autoimmunity illustrate this mechanism. Similarly, changes in gut microbiota that lead to dysbiosis and an increased Bacteroidetes-to-Firmicutes ratio have been linked to seroconversion and the onset of T1D. The microbiota plays a role in shaping peripheral immune tolerance by modulating the migration and differentiation of immune cells, helping to maintain intestinal homeostasis. Additionally, local inflammation is mitigated by short-chain fatty acids (SCFAs) produced by gut bacteria during the fermentation of non-digestible carbohydrates [18].

Moreover, a breastfeeding duration of less than 12 months and a positive family history of type 1 or type 2 diabetes are associated with a higher risk of developing T1D. The frequency of stressful life events during pregnancy was also higher among mothers of children with diabetes. However, no association was found between maternal smoking or alcohol consumption during pregnancy and type 1 diabetes [12].

Clinical Manifestations

Diabetes type 1 have many clinical manifestations, lots of the symptoms are non-specific, that's why many patients don't seek medical care immediately when first signs appear. The typical symptoms include: polyuria, polydipsia, nocturnal enuresis, blurred vision, unintentional weight loss, fatigue, weakness and slow-healing wounds. In near 90% of case diabetes type 1 is diagnosed in children, when they are admitted to the hospital with DKA's symptoms (belly pain, vomiting, fruity breath, nausea, loss of appetite, headache, confusion) as a first presentation of their disease. In adult-onset DKA hardly ever is a first symptom, more often it is as result of improper treatment of diabetes [23]. What is as important to remember as symptoms of diabetes is long-term related complications. They are divided into microvascular and macrovascular.
Microvascular:

- Retinopathy, which appears to represent the most frequen cause of blindness among adults.

- Nephropathy has been reported to occur in 20-40% of patients with diabetes and is the leading cause of end-stage renal disease. Microalbuminuria is the first manifestation of this complication.
- Neuropathy is usually presented as chronic sensorimotor diabetic peripheral neuropathy and autonomic neuropathy.

Unfortunately, when it comes to macrovascular complications there have been less studied and less is known about specific determinants of disease particular to T1D. What is known is that type 1 diabetes increase risk of cardiovascular disease and cerebrovascular accidents [24].

What is more, we should remember about hypoglycemia as a result of skipping or delaying meals, taking too much insulin. Intense exercise and failing to adjust your food or insulin intake can also be triggers for it. If episodes appear regular, they can influence the brain and lead to neuroglycopenia [25].

The impact of diet on type 1 diabetes

The recommended model for treating type 1 diabetes is intensive insulin therapy using pens or continuous subcutaneous insulin infusion [26]. As demonstrated by the results of the Diabetes Control and Complications Trial, this model, despite its many advantages, has two main adverse treatment effects—more frequent episodes of hypoglycemia in patients treated with this method and greater weight gain compared to those using conventional insulin therapy [27]. Surprisingly, an increasing number of individuals with type 1 diabetes are struggling with overweight or obesity, despite the fact that the clinical symptoms of type 1 diabetes have traditionally been associated with weight loss [28]. As evidenced by the results of the Diabetes Control and Complications Trial, the average BMI (body mass index) of individuals with type 1 diabetes at the beginning of observation was 23 kg/m², and after nine years, it increased to 26 kg/m² [29]. Furthermore, the results of some studies indicate the occurrence of "double diabetes" in patients with type 1 diabetes, characterized by insulin resistance and features of autoimmune diabetes [30]. The coexistence of insulin resistance and type 1 diabetes negatively impacts metabolic control and the development of chronic complications.

Typical dietary patterns used in the management of prediabetes and type 2 diabetes are not directly applicable to type 1 diabetes. There is no literature confirming the specific effects of the Mediterranean, vegetarian or vegan, low-fat, DASH, or Paleo diets in the management of type 1 diabetes. Moreover, there is only limited evidence regarding the impact of fasting on type 1 diabetes [31]. Nonetheless, an appropriate diet is crucial for improving overall health as well as in the prevention and treatment of chronic diabetes complications [32]. As with healthy individuals, dietary recommendations for people with type 1 diabetes should consider age, gender, level of physical activity, economic status, and food preferences [33].

The most important dietary component, from the perspective of the patient and adjusting the appropriate insulin dose, is carbohydrates, which have the most significant impact on postprandial glycemia [34]. The primary source of carbohydrates in the diet should be whole-grain products characterized by a low glycemic index (GI < 55). Products with a high glycemic index (GI > 70) require higher insulin doses and are more likely to cause weight gain due to the anabolic effect of insulin [35].

Fats should constitute 30–35% of the total energy value in the diet of individuals with type 1 diabetes. It is important to ensure that the sources of these fats are appropriate. Saturated fats should constitute less than 10% of the total energy value of the diet, while the main sources of fats should be products rich in monounsaturated and polyunsaturated fats, which should account for 10–15% and 6–10% of the total energy value, respectively [36]. Additionally, dietary cholesterol should not exceed 300 mg/dl, and in individuals with elevated LDL cholesterol levels, it should not exceed 200 mg/dl. Trans fatty acids should be minimized as much as possible, as they have a negative impact on the cardiovascular system, contribute to insulin resistance, and accelerate the atherosclerotic process [37].

The "gold standard" in dietary management of diabetes for patients who also require weight reduction remains a low-carbohydrate diet. Krebs et al. evaluated the impact of a low-carbohydrate diet on weight loss, metabolic control, and daily insulin dose in adults with type 1 diabetes. The authors observed that in patients on a low-carbohydrate diet, HbA1c levels decreased (from 7.9 to 7.2 mmol/l), indicating improved metabolic control (no changes were observed in the control group). Furthermore, the daily insulin dose was reduced, and the BMI decreased from 27 kg/m² to 25 kg/m² in the study group [38].

Several studies have examined the impact of a very low-carbohydrate diet on adults with type 1 diabetes. In one randomized crossover trial involving 10 participants, a very low-carbohydrate diet, consisting of 47 grams of carbohydrates per day, without calorie restriction, was compared with a higher carbohydrate diet, consisting of 225 grams per day, over a one-week period. The results showed that individuals on the very low-carbohydrate diet experienced less glycemic variability, spent more time in euglycemia, less time in hypoglycemia, and required lower insulin doses [39]. In another study, a single-arm trial involving 48 participants, the goal of consuming 75 grams or less of carbohydrates per day resulted in weight loss, reduced A1C levels, and triglycerides, as well as increased HDL-C levels after three months. Even after four years, A1C levels remained lower, and HDL-C levels remained higher compared to baseline values [40]. These findings suggest that a very low-carbohydrate diet may offer potential benefits for adults with type 1 diabetes**.**

Physical Activity

Physical activity plays a crucial role in human life. For many years, it was believed that individuals with diabetes should avoid excessive physical exertion. Currently, however, the medical community recognizes physical activity as an integral and essential component of diabetes treatment [41]. The primary energy source for working muscles is glucose, derived both from dietary intake and from processes such as glycogenolysis and gluconeogenesis [42]. Maintaining energy balance during training largely depends on hormones like insulin, catecholamines, glucagon, glucocorticosteroids, and growth hormone. The preferred form of physical activity for individuals with diabetes is aerobic exercise (endurance training), during which glucose is oxidized in the presence of oxygen [43].

In individuals with type 1 diabetes, during physical activity, the concentration of exogenous insulin in the blood is not physiologically regulated, which increases the risk of hypoglycemia—the most significant hazard for those engaging in sports [44]. The occurrence of hypoglycemia depends on the type of insulin, its dosage, glycemic levels, the amount of carbohydrates consumed before exercise, as well as the type and duration of the training. Conversely, very intense exercises, especially anaerobic ones, can lead to increased glycemic levels due to the surge of adrenaline, noradrenaline, cortisol, glucagon, and growth hormone, as well as stress associated with competition [45]. Hyperglycemia can also result from errors

stemming from the fear of hypoglycemia, such as consuming an excessive amount of carbohydrates relative to the administered insulin. Therefore, self-monitoring of glycemia, involving regular blood glucose checks using a glucometer before, during, and after training, is a crucial component of therapy in athletes with diabetes [46].

Due to the risk of diabetic ketoacidosis, individuals with type 1 diabetes should avoid physical activity when blood glucose levels exceed 250 mg/dl (13.9 mmol/l) and ketone bodies are present in the urine. Exercise is also not recommended when, despite the absence of acetone in the urine, glycemia exceeds 300 mg/dl (16.7 mmol/l) [47].

Limitations to increased physical activity also arise from advanced diabetic complications. Physical exertion in individuals with proliferative retinopathy carries the risk of vitreous hemorrhage and retinal detachment. Training in patients with diabetic nephropathy can increase urinary albumin excretion and accelerate the progression of this complication [48]. Autonomic neuropathy is associated with orthostatic hypotension, resting tachycardia, and thermoregulatory disorders; thus, exercise in extreme temperatures is not recommended for individuals with this condition. In the case of diabetic foot syndrome, there is an increased risk of injuries, including bone fractures due to coexisting osteoporosis. Moreover, in individuals with vascular complications of diabetes, physical exertion can lead to silent myocardial ischemia [49].

The type of physical activity recommended for individuals with type 1 diabetes should be tailored based on age, disease duration, previous physical fitness, and the presence and severity of chronic complications. Patients engaging in physical activity should receive comprehensive training in intensive functional insulin therapy. For individuals leading a sedentary lifestyle, especially in the presence of other risk factors for ischemic heart disease, it is advised to perform an ECG stress test before making lifestyle changes and initiating training.

Conclusions

Type 1 diabetes is characterized by the early apoptosis of pancreatic β-cells, which can occur even before clinical symptoms manifest. The pathogenesis of the disease involves β-cell autoimmunity, as evidenced by the presence of autoantibodies and insulitis. This autoimmune destruction of β-cells results from a complex interplay of genetic and environmental factors, although the precise triggers are not yet fully understood. The disease progresses through three stages: asymptomatic autoimmunity, asymptomatic autoimmunity with dysglycemia, and symptomatic diabetes with clinical manifestations.

The mechanisms underlying β-cell destruction include the presence of autoantibodies targeting islet cells and insulin, which indicate an increased risk of developing diabetes. The immune response, involving cytokines and autoreactive T lymphocytes, exacerbates β-cell destruction. Additionally, disruptions in thymic education contribute to the autoimmune attack on insulin-producing cells. Genetic predisposition plays a significant role, with HLA DR and DQ genotypes being strongly associated with Type 1 diabetes. Recent advances in genetic risk assessment, such as genetic risk scores (GRS) and polygenic risk scores (PRS), have enhanced the understanding of inherited risk factors. Environmental factors also play a crucial role in the development of Type 1 diabetes. Viral infections, changes in gut microbiota, and dietary factors are known to influence β-cell susceptibility and the development of autoimmunity.

Based on the literature analysis, it can be concluded that an appropriate diet, particularly a low-carbohydrate diet, plays a crucial role in managing type 1 diabetes by improving glycemic control, reducing body weight, and decreasing the need for insulin. Despite the limited number of studies, the results suggest potential benefits of carbohydrate restriction in the diet of patients with type 1 diabetes, which may help reduce the risk of disease-related complications.

It is evident that physical activity, when carefully managed and tailored to individual needs, plays a vital role in the comprehensive management of type 1 diabetes, contributing to improved glycemic control and overall health. However, specific considerations and precautions must be taken to mitigate the risks associated with hypoglycemia, hyperglycemia, and other diabetes-related complications during exercise.

Disclosure:

Authors' contribution:

Conceptualization: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Methodology: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Software: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Check: Agata Konopka, Weronika Smołka
Formal Analysis: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Investigation: Weronika Smołka, Marcin Skrzypczyk
Resources: Marcin Skrzypczyk, Leon Smółka
Data Curation: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Writing-Rough Preparation: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Writing-Review and Editing: Agata Konopka, Weronika Smołka, Marcin Skrzypczyk, Leon Smółka
Visualization: Agata Konopka, Weronika Smołka
Supervision: Marcin Skrzypczyk, Leon Smółka
Project Administration: Marcin Skrzypczyk, Leon Smółka

All authors have read and agreed with the published version of the manuscript.

Funding statement:
The study did not receive special funding.

Institutional review board statement:
Not applicable.

Informed consent statement:
Not applicable.

Data availability statement:
Not applicable.

Conflict of interest:
The authors declare no conflict of interest

References:

1. National Collaborating Centre for Women's and Children's Health (UK). Diabetes (Type 1 and Type 2) in Children and Young People: Diagnosis and Management.

London: National Institute for Health and Care Excellence (UK); 2015 Aug. PMID: 26334077.
2. Daneman D. Type 1 diabetes. Lancet. 2006 Mar 11;367(9513):847-58. doi: 10.1016/S0140-6736(06)68341-4. PMID: 16530579.
3. Zahalka SJ, Abushamat LA, Scalzo RL, Reusch JEB. The Role of Exercise in Diabetes. 2023 Jan 6. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, de Herder WW, Dhatariya K, Dungan K, Hofland J, Kalra S, Kaltsas G, Kapoor N, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, New M, Purnell J, Sahay R, Shah AS, Singer F, Sperling MA, Stratakis CA, Trence DL, Wilson DP, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–. PMID: 31751111.
4. Cartee GD. Mechanisms for greater insulin-stimulated glucose uptake in normal and insulin-resistant skeletal muscle after acute exercise. Am J Physiol Endocrinol Metab. 2015 Dec 15;309(12):E949-59. doi: 10.1152/ajpendo.00416.2015. Epub 2015 Oct 20. PMID: 26487009; PMCID: PMC4816200.
5. IDF Diabetes Atlas [Internet]. [Cited: 07.07.2024]. Available from: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf
6. Gregory GA, Robinson TIG, Linklater SE, Wang F, Colagiuri S, de Beaufort C, Donaghue KC; International Diabetes Federation Diabetes Atlas Type 1 Diabetes in Adults Special Interest Group; Magliano DJ, Maniam J, Orchard TJ, Rai P, Ogle GD. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Lancet Diabetes Endocrinol. 2022 Oct;10(10):741-760. doi: 10.1016/S2213-8587(22)00218-2. Epub 2022 Sep 13. Erratum in: Lancet Diabetes Endocrinol. 2022 Nov;10(11):e11. doi: 10.1016/S2213-8587(22)00280-7. PMID: 36113507.
7. Epidemiology of diabetes in Poland in 2014–2017 [Internet]. [Cited: 07.07.2024]. Available from: https://basiw.mz.gov.pl/wp-content/uploads/2020/06/Epidemiologia-cukrzycy-w-Polsce-w-latach-2014-2017.pdf
8. Ogrotis I, Koufakis T, Kotsa K. Changes in the Global Epidemiology of Type 1 Diabetes in an Evolving Landscape of Environmental Factors: Causes, Challenges, and Opportunities. Medicina (Kaunas). 2023 Mar 28;59(4):668. doi: 10.3390/medicina59040668. PMID: 37109626; PMCID: PMC10141720.
9. Stene LC, Norris JM, Rewers MJ. Risk Factors for Type 1 Diabetes. 2023 Dec 20. In: Lawrence JM, Casagrande SS, Herman WH, et al., editors. Diabetes in America [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); 2023-.
10. (Zajec A, Trebušak Podkrajšek K, Tesovnik T, Šket R, Čugalj Kern B, Jenko Bizjan B, Šmigoc Schweiger D, Battelino T, Kovač J. Pathogenesis of Type 1 Diabetes: Established Facts and New Insights. Genes (Basel). 2022 Apr 16;13(4):706. doi: 10.3390/genes13040706. PMID: 35456512; PMCID: PMC9032728.
11. Chwalba A, Pilśniak A, Otto-Buczkowska E. β-cell self-destruction and extremely complicated and still unknown etiopathogenesis of type 1 diabetes. Pediatr Endocrinol Diabetes Metab. 2021;27(1):47-50. doi: 10.5114/pedm.2020.103058. PMID: 33599437; PMCID: PMC10227476.
12. Boljat A, Gunjača I, Konstantinović I, Vidan N, Boraska Perica V, Pehlić M, Škrabić V, Zemunik T. Environmental Risk Factors for Type 1 Diabetes Mellitus Development. Exp Clin Endocrinol Diabetes. 2017 Sep;125(8):563-570. doi: 10.1055/s-0043-109000. Epub 2017 Jul 27. PMID: 28750427.

13. Akil AA, Yassin E, Al-Maraghi A, Aliyev E, Al-Malki K, Fakhro KA. Diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era. J Transl Med. 2021 Apr 1;19(1):137. doi: 10.1186/s12967-021-02778-6. PMID: 33794915; PMCID: PMC8017850.
14. Eisenbarth GS, Jeffrey J. The natural history of type 1A diabetes. Arq Bras Endocrinol Metabol. 2008 Mar;52(2):146-55. doi: 10.1590/s0004-27302008000200002. PMID: 18438525.
15. Miao D, Yu L, Eisenbarth GS. Role of autoantibodies in type 1 diabetes. Front Biosci. 2007 Jan 1;12:1889-98. doi: 10.2741/2195. PMID: 17127428.
16. (Eizirik DL, Pasquali L, Cnop M. Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure. Nat Rev Endocrinol. 2020 Jul;16(7):349-362. doi: 10.1038/s41574-020-0355-7. Epub 2020 May 12. PMID: 32398822.
17. Mannering SI, Di Carluccio AR, Elso CM. Neoepitopes: a new take on beta cell autoimmunity in type 1 diabetes. Diabetologia. 2019 Mar;62(3):351-356. doi: 10.1007/s00125-018-4760-6. Epub 2018 Nov 6. PMID: 30402774.
18. Roep BO, Thomaidou S, van Tienhoven R, Zaldumbide A. Type 1 diabetes mellitus as a disease of the β-cell (do not blame the immune system?). Nat Rev Endocrinol. 2021 Mar;17(3):150-161. doi: 10.1038/s41574-020-00443-4. Epub 2020 Dec 8. PMID: 33293704; PMCID: PMC7722981.
19. Oram RA, Redondo MJ. New insights on the genetics of type 1 diabetes. Curr Opin Endocrinol Diabetes Obes. 2019 Aug;26(4):181-187. doi: 10.1097/MED.0000000000000489. PMID: 31219823.
20. Minniakhmetov I, Yalaev B, Khusainova R, Bondarenko E, Melnichenko G, Dedov I, Mokrysheva N. Genetic and Epigenetic Aspects of Type 1 Diabetes Mellitus: Modern View on the Problem. Biomedicines. 2024 Feb 8;12(2):399. doi: 10.3390/biomedicines12020399. PMID: 38398001; PMCID: PMC10886892.
21. Luckett AM, Weedon MN, Hawkes G, Leslie RD, Oram RA, Grant SFA. Utility of genetic risk scores in type 1 diabetes. Diabetologia. 2023 Sep;66(9):1589-1600. doi: 10.1007/s00125-023-05955-y. Epub 2023 Jul 13. PMID: 37439792; PMCID: PMC10390619.
22. Powers AC. Type 1 diabetes mellitus: much progress, many opportunities. J Clin Invest. 2021 Apr 15;131(8):e142242. doi: 10.1172/JCI142242. PMID: 33759815; PMCID: PMC8262558.
23. Syed FZ. Type 1 Diabetes Mellitus. Ann Intern Med. 2022 Mar;175(3):ITC33-ITC48. doi: 10.7326/AITC202203150. Epub 2022 Mar 8. PMID: 35254878.
24. Melendez-Ramirez LY, Richards RJ, Cefalu WT. Complications of type 1 diabetes. Endocrinol Metab Clin North Am. 2010 Sep;39(3):625-40. doi: 10.1016/j.ecl.2010.05.009. PMID: 20723824.
25. Lucier J, Weinstock RS. Type 1 Diabetes. 2023 Mar 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 29939535.
26. Salsali, Afshin; Nathan, Muriel. A Review of Types 1 and 2 Diabetes Mellitus and Their Treatment with Insulin. American Journal of Therapeutics 13(4)349-361, July 2006.
27. Nathan D. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview. Diabetes Care. 2013; 37(1): 9–16, doi: 10.2337/dc13- 2112
28. Minges KE, Whittemore R, Grey M. Overweight and obesity in youth with type 1 diabetes. Annu Rev Nurs Res. 2013; 31: 47–69, doi: 10.1891/0739-6686.31.47, indexed in Pubmed: 24894137.

29. Conway B, Miller RG, Costacou T, et al. Temporal patterns in overweight and obesity in Type 1 diabetes. Diabet Med. 2010; 27(4): 398–404, doi: 10.1111/j.1464-5491.2010.02956.x, indexed in Pubmed: 20536510
30. Pozzilli, Paolo, and Raffaella Buzzetti. "A new expression of diabetes: double diabetes." Trends in Endocrinology & Metabolism 18.2 (2007): 52-57.
31. Musil F, Smahelová A, Bláha V, et al. Effect of low calorie diet and controlled fasting on insulin sensitivity and glucose metabolism in obese patients with type 1 diabetes mellitus. Physiol Res 2013;62:267–276
32. Deed, G., Barlow, J., Kawol, D., Kilov, G., Sharma, A., & Yu Hwa, L. (2015). Diet and diabetes. Australian Family Physician, 44(5), 288–292
33. Juruć A, Pisarczyk-Wiza D, Wierusz-Wysocka B. Zalecenia dietetyczne i zachowania żywieniowe u osób z cukrzycą typu 1 — czy mają wpływ na kontrolę metaboliczną? Diabet Klin. 2014; 3(1): 22–30
34. Kendall, C., Josse, A., Esfahani, A. et al. The impact of pistachio intake alone or in combination with high-carbohydrate foods on post-prandial glycemia. Eur J Clin Nutr 65, 696–702 (2011). https://doi.org/10.1038/ejcn.2011.12
35. Klupa T. Żywienie w cukrzycy typu 1. In: Sieradzki J, Wierusz-Wysocka B. ed. Cukrzyca typu 1 u osób dorosłych. Termedia Wydawnictwa Medyczne, Poznań 2012: 129–137
36. Rosenfalck, A. M., et al. "A low-fat diet improves peripheral insulin sensitivity in patients with Type 1 diabetes." Diabetic medicine 23.4 (2006): 384-392
37. Piłaciński S, Zozulińska-Ziółkiewicz DA. Influence of lifestyle on the course of type 1 diabetes mellitus. Arch Med Sci. 2014; 10(1): 124–134, doi: 10.5114/aoms.2014.40739
38. Krebs JD, Parry Strong A, Cresswell P, et al. A randomised trial of the feasibility of a low carbohydrate diet vs standard carbohydrate counting in adults with type 1 diabetes taking body weight into account. Asia Pac J Clin Nutr. 2016; 25(1): 78–84
39. Ranjan A, Schmidt S, Damm-Frydenberg C, Holst JJ, Madsbad S, Nørgaard K. Short-term effects of a low carbohydrate diet on glycaemic variables and cardiovascular risk markers in patients with type 1 diabetes: a randomized open-label crossover trial. Diabetes Obes Metab 2017;19:1479–1484
40. Nielsen JV, Gando C, Joensson E, Paulsson C. Low carbohydrate diet in type 1 diabetes, long-term improvement and adherence: a clinical audit. Diabetol Metab Syndr 2012;4:23
41. Waden J., Tikkanen H., Forsblom C. et al. Leisure time physical activity is associated with poor glycemic control in type 1 diabetic women. Diabetes Care 2005; 28: 777–782
42. Di Mauro, S. "Muscle glycogenoses: an overview." Acta Myologica 26.1 (2007): 35
43. Chimen, Myriam, et al. "What are the health benefits of physical activity in type 1 diabetes mellitus? A literature review." Diabetologia 55 (2012): 542-551
44. Kalinowski P, Bojakowska U, Kowalska ME. Assessment of patients' knowledge about the complications of diabetes. Med Og Nauk Zdr. 2012;18(4):302-307
45. Hargreaves M., Angus D., Howlett K., Conus N.M., Febbraio M. Effect of heat stress on glucose kinetics during exercise. J. Appl. Physiol. 1996; 81: 1594–1597
46. Kirk, Susan E. "Hypoglycemia in athletes with diabetes." Clinics in sports medicine 28.3 (2009): 455-468
47. Clinical recommendations for the management of patients with diabetes. Position of the Polish Diabetes Association, Diab Dośw I Klin 11 (2011)

48. Ren, C., Liu, W., Li, J. et al. Physical activity and risk of diabetic retinopathy: a systematic review and meta-analysis. Acta Diabetol 56, 823–837 (2019). https://doi.org/10.1007/s00592-019-01319-4
49. Standards of Medical Care in Diabetes 2010. Diabetes Care 2010; 33: 11–61