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Parameters influencing Type 1 and Type 2 diabetes mellitus

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ABSTRACT

Diabetes mellitus, a long-term condition impacting millions globally, is mainly categorized into Type 1 (T1D) and Type 2 diabetes mellitus (T2D), each with distinct etiological pathways but sharing the common trait of high blood glucose levels. T1DM is marked by the autoimmune destruction of insulin-producing β-cells in the pancreas, resulting in total insulin deficiency. This condition commonly affects younger individuals and has strong genetic and environmental determinants, including specific genetic markers like HLA variants and exposure to certain viral infections. T2DM, conversely, is primarily influenced by insulin resistance and a relative lack of insulin. This type typically presents in adults and is influenced by multiple factors like obesity, sedentary lifestyle, age, and genetic predispositions. While both types of diabetes ultimately result in hyperglycemia and similar complications, their underlying mechanisms and contributing factors are notably different. Understanding these parameters is critical for improving diagnosis, management, and prevention strategies. This article reviews the key parameters influencing T1DM and T2DM, focusing on genetic, autoimmune, environmental, and lifestyle factors. Through this understanding, healthcare providers and researchers can advance specific interventions and management approaches that cater to the distinct requirements of each type of diabetes, potentially reducing the global burden of this condition.

KEYWORDS

Diabetes Mellitus; Type 1 Diabetes; Type 2 Diabetes; Genetic Influences; Insulin Resistance

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Introduction

Diabetes mellitus, often known simply as diabetes, represents a significant health challenge due to its prevalence, complexity, and potential for severe complications. Type 1 diabetes (T1DM) and Type 2 diabetes (T2DM) are the primary types of diabetes, each possessing distinct pathophysiological and clinical features [1]. T1DM is generally understood as an autoimmune disorder leading to a complete lack of insulin caused by the destruction of β-cells in the pancreas [2]. T2DM, however, is more complex and often arises from a combination of insulin resistance and progressive β-cell dysfunction, largely influenced by lifestyle and metabolic factors [3]. Although both types lead to elevated blood glucose levels, they differ in etiology, age of onset, and the parameters that contribute to disease development. This article explores the genetic, environmental, autoimmune, and lifestyle parameters influencing both types of diabetes, providing insights into the factors that drive these conditions and potential avenues for treatment and prevention.

Genetic Factors in Type 1 and Type 2 Diabetes

Genetics play a central role in determining susceptibility to both T1DM and T2DM, although the mechanisms and extent of influence vary. T1DM, known for its autoimmune nature, is heavily influenced by genetic predisposition linked to immune system regulation [4]. The HLA region located on chromosome 6 is especially significant, as certain HLA class II alleles, including HLA-DR3, HLA-DR4, and HLA-DQ, have been found to considerably elevate the risk of developing T1DM [5]. The presence of these specific HLA variants contributes to a heightened immune response, which can lead to the targeting and destruction of pancreatic β-cells. Nevertheless, not everyone who possesses these genetic markers will develop T1DM, indicating a necessary interaction between genetics and environmental triggers for disease onset.

In T2DM, the genetic influence is more diffuse and complex. Unlike T1DM, T2DM is polygenic, involving numerous genes that collectively impact insulin production, release, and responsiveness. Genes like TCF7L2, which affects insulin secretion and β-cell function, and PPARG, which influences adipocyte differentiation and lipid metabolism, are known to elevate the risk of T2DM. Genome-wide association studies (GWAS) have discovered more than 400 genetic loci linked to T2DM, underscoring its polygenic nature. Unlike T1DM, these genetic variants do not typically lead to diabetes in isolation but significantly increase susceptibility when combined with lifestyle risk factors like obesity and physical inactivity [6]. Additionally, certain ethnic groups, such as those of South Asian or Hispanic descent, exhibit higher genetic predispositions to T2DM, making population-specific genetic research important for recognizing at-risk individuals and tailoring preventive measures.

Autoimmunity and Inflammation in Diabetes

Autoimmunity is the primary pathological process in T1DM, distinguishing it sharply from the inflammatory processes that

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drive T2DM. In T1DM, the immune system erroneously recognizes β-cells in the pancreas as foreign, launching an attack that ultimately leads to the destruction of these insulin-producing cells [7]. This autoimmune reaction is characterized by the presence of various autoantibodies, including those targeting glutamic acid decarboxylase (GAD), insulin, and IA-2. These autoantibodies can often be detected years before clinical symptoms arise, offering a window for early diagnosis and potential interventions. While the exact triggers for this autoimmune process remain elusive, viral infections particularly with enteroviruses have been implicated as possible catalysts that activate immune responses in genetically predisposed individuals. Other hypotheses suggest that factors such as gut microbiota dysbiosis or exposure to certain dietary proteins in early childhood might contribute to the development of T1DM [8].

In T2DM, although autoimmunity is not involved, inflammation significantly contributes a critical role in exacerbating insulin resistance and disease progression. Adipose tissue, especially visceral fat, acts as an active endocrine organ and secretes pro-inflammatory cytokines, such as TNF-α, IL-6, and CRP, which interfere with insulin signaling pathways [9]. This persistent low-level inflammation is frequently observed in people with obesity, a major risk factor for T2DM. Over time, these inflammatory markers impair insulin receptor function on cells, reducing their ability to respond to insulin and causing blood glucose levels to rise [10]. The interplay between inflammation and metabolic stress in T2DM not only worsens insulin resistance but also places a continuous burden on pancreatic β-cells, hastening their decline in function [11]. Furthermore, Inflammation in T2DM is likewise linked to a heightened risk of cardiovascular complications, making it a critical area for therapeutic intervention [12].

Environmental and Lifestyle Factors

Environmental factors exert a profound influence on both T1DM and T2DM, though the specific factors and their impacts differ between the two types. In T1DM, early-life exposures like viral infections, geographic location, and dietary components are thought to act as triggers in genetically predisposed individuals [13]. For instance, studies have shown that exposure to certain viral infections—particularly enteroviruses and coxsackievirus—may increase the likelihood of initiating the autoimmune process that leads to β-cell destruction [14]. Geographic studies have also revealed that the incidence of T1DM is higher in countries at northern latitudes, which has helped researchers explore the potential role of vitamin D deficiency due to lower sunlight exposure in these regions. Dietary exposures in infancy, such as early introduction to cow's milk or gluten, have also been proposed as possible risk factors, although findings are inconclusive [15]. Research is ongoing to clarify the role of these environmental factors and identify modifiable triggers that may help reduce the incidence of T1DM.

For T2DM, environmental factors are intricately linked to lifestyle and behavioral choices that directly influence metabolic health. The modern lifestyle, characterized by sedentary behavior, high-calorie diets, and limited physical activity, has driven a global surge in T2DM prevalence. Obesity, one of the strongest risk factors for T2DM, often results from excessive calorie intake coupled with insufficient physical activity. Adiposity, especially visceral fat, contributes to insulin resistance, as fat cells release free fatty acids and inflammatory mediators that interfere with insulin signaling [16]. Beyond obesity, other lifestyle factors such as poor sleep quality, chronic stress, and limited access to nutritious food also contribute to the development of T2DM. Urbanization and socioeconomic factors exacerbate these risks, as urban environments often promote unhealthy diets and physical inactivity. Therefore, public health interventions targeting lifestyle modification, including promoting physical activity, encouraging balanced diets, and improving access to healthy food, are essential for preventing T2DM.

Role of Insulin Resistance and β-Cell Dysfunction

Insulin resistance and β-cell impairment are key aspects of the pathophysiology of T2DM, but they also play roles, albeit differently, in T1DM [17]. In T2DM, insulin resistance typically arises in muscle, liver, and fat cells. When these tissues develop resistance to insulin, the pancreas responds by generating more insulin to keep blood glucose levels normal. However, as insulin resistance progresses, β-cells cannot meet the required demand, leading to a gradual decline in insulin secretion capacity. Factors such as obesity, particularly visceral obesity, perform a pivotal role in promoting insulin resistance. Visceral fat is metabolically active and produces free fatty acids, hormones, and inflammatory cytokines that impair insulin action. Additionally, ectopic fat deposition in organs like the liver and pancreas further exacerbates insulin resistance and hampers β-cell function, creating a cycle of worsening hyperglycemia and β-cell stress [18].

In T1DM, β-cell dysfunction is an absolute rather than a relative loss due to the autoimmune destruction of these cells. Although T1DM is primarily defined by the lack of insulin production, some studies have observed that even individuals with T1DM can develop insulin resistance, especially if they become overweight or inactive [19]. This condition, sometimes referred to as "double diabetes," combines aspects of both T1DM and T2DM and presents unique challenges for management, as affected individuals require both insulin therapy and strategies to manage insulin resistance. Interestingly, β-cell dysfunction in both T1DM and T2DM may be influenced by glucotoxicity and lipotoxicity, where elevated glucose and lipid levels exert toxic effects on β-cells, hastening their decline [20]. This complex interplay between insulin resistance, β-cell stress, and metabolic dysfunction underscores the need for comprehensive management strategies that address both insulin action and β-cell health in diabetes care.

Conclusions

Type 1 and Type 2 diabetes are influenced by a complex interplay of genetic, autoimmune, environmental, and lifestyle elements. T1DM is primarily driven by autoimmune mechanisms in genetically predisposed individuals, with environmental triggers potentially initiating or accelerating the process of β-cell destruction. T2DM, on the other hand, is mainly impacted by insulin resistance and lifestyle elements like

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diet, exercise, and obesity, although genetic predisposition is also significant. These distinct yet overlapping parameters highlight the need for personalized approaches in diabetes management, with targeted interventions addressing the specific etiological factors of each type. As studies keep revealing the genetic and environmental foundations of diabetes, there is optimism for more targeted prevention methods. By addressing these diverse influences, doctors and scientists can make progress in lowering the impact of diabetes and enhancing life quality for those impacted.

Disclosure statement

No potential conflict of interest was reported by the authors.

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