Journal of Medicine and Medical Sciences Vol. 14(1) pp. 1-3, January, 2023
Available online https://www.interesjournals.org/medicine-medical-sciences.html

Review Article

Diabetes and Metabolism: Type 2 Diabetes Mellitus

Panayides Andreas*

Department of Computer Science, University of Cyprus, Nicosia, Cyprus

*Corresponding Author's E-mail: andreas.p@edu.cp

Received: 02-Jan-2023; Manuscript No: jmms-23-87045; **Editor assigned:** 3-Jan-2023; Pre-QC No: jmms-23-87045 (PQ); **Reviewed:** 16-Jan-2023; QC No: jmms-23-87045; **Revised:** 23-Jan-2023; Manuscript No: jmms-23-87045 (R); **Published:** 30-Jan-2023, DOI: 10.14303/2141-9477.2023.17

Abstract

One of the most prevalent metabolic disorders, Type 2 Diabetes (T2DM), is brought on by a combination of two primary factors: the inability of insulin-sensitive tissues to respond appropriately to insulin and defective insulin secretion by pancreatic cells. The molecular mechanisms involved in insulin synthesis, release, and detection are tightly regulated because insulin release and activity are necessary for glucose homeostasis. A metabolic imbalance that is the cause of the disease can result from flaws in any of the mechanisms involved in these processes. The key features of type 2 diabetes and the molecular mechanisms and pathways that are thought to play a role in insulin metabolism and lead to insulin resistance and T2DM are the subject of this review. In order to accomplish this, we present a summary of the data that has been collected thus far, with a particular emphasis on insulin synthesis, insulin release, insulin sensing, and the subsequent effects on distinct insulin-sensitive organs. The pathological conditions that exacerbate T2DM are also discussed, including metabolic memory, gut dysbiosis, and nutritional factors. We also discuss some of the molecular mechanisms that link T2DM and Insulin Resistance (IR), as well as cardiovascular risk, which is one of the most significant T2DM complications. This is because T2DM is linked to the acceleration of the development of atherosclerosis.

Keywords: Type 2 Diabetes Mellitus, Insulin Resistance, β-cell, Liver, Adipocyte, Muscle, Cardiovascular Disease, Pathophysiology

INTRODUCTION

One of the most prevalent metabolic disorders worldwide, Type 2 Diabetes Mellitus (T2DM) is primarily brought about by a combination of two main factors: insulin resistance in insulin-sensitive tissues and malfunctioning insulin secretion by pancreatic cells The metabolic demand must be precisely met by insulin release and action; As a result, the insulin response in tissues and the molecular mechanisms involved in insulin synthesis and release must be tightly controlled. As a result, the pathogenesis of T2DM can be caused by a metabolic imbalance caused by flaws in any of the involved mechanisms (Boni MF et al., 2020).

The molecular mechanisms and pathways involved in insulin metabolism, as well as the connections between T2DM and cardiovascular pathophysiology, are all examined in this review. Global T2DM trends and the roles of major risk factors, particularly obesity, lifestyle factors, genetic predispositions, gut dysbiosis, epigenetics, and mitochondrial deregulation, are discussed in this review (Latinne A et al., 2020).

Diabetes mellitus, as defined by the World Health Organization (WHO), is a metabolic, chronic condition characterized by elevated blood glucose levels that eventually cause damage to the heart, vasculature, eyes, kidneys, and nerves. T2DM, which is characterized by a lack of insulin secretion by pancreatic islet cells, tissue Insulin Resistance (IR), and an inadequate compensatory insulin secretory response, accounts for more than 90% of cases of diabetes mellitus. As the disease progresses, insulin secretion becomes unable to regulate glucose homeostasis, resulting in hyperglycaemia. Obesity or a higher body fat percentage, primarily in the abdominal area, is the main characteristics of T2DM patients. Adipose tissue promotes

Insulin Resistance (IR) in this condition through a variety of inflammatory mechanisms, such as increased release of Free Fatty Acids (FFA) and regulation of adipocytes. The global rise in obesity, sedentary lifestyles, high-calorie diets, and population aging, which has quadrupled the incidence and prevalence of T2DM, are the primary drivers of the epidemic. The pancreas (cells and -cells), liver, skeletal muscle, kidneys, brain, small intestine, and adipose tissue are all involved in the development of T2DM. Adipokine deregulation, inflammation, and abnormalities in the microbiota of the gut have emerged as significant pathophysiological factors, according to evolving data (Andersen KG et al., 2020).

DISCUSSION

Risk and Genetic Predisposition

The complex combination of genetic, metabolic, and environmental risk factors that contribute to T2DM's prevalence interact with one another. Although non-modifiable risk factors (ethnicity and family history/genetic predisposition) have a strong genetic basis for individual T2DM predisposition, epidemiological studies suggest that improving the main modifiable risk factors (obesity, low physical activity, and unhealthy diet) can prevent many cases of T2DM (Lau SKP et al., 2007) .

The risk of developing T2DM is significantly influenced by genetic predisposition. Numerous T2DM genome-wide association studies over the past ten years have demonstrated the complex polygenic nature of T2DM. The majority of these loci increase T2DM risk through primary effects on insulin secretion, while a small number reduce insulin action. Dimas and co. grouped these variants according to the potential intermediate mechanisms they might play in the pathophysiology of T2DM, with four of them following a distinct IR pattern; two, fasting hyperglycemia reducing insulin secretion; nine normal fasting glycaemia lowering insulin secretion; and one that changes how insulin is made. These data indicate that the genetic architecture of T2DM is highly polygenic, and the majority of T2DM loci require additional association studies. As demonstrated by observational studies and clinical trials, interactions between susceptibility loci and environmental factors may account for the absence of T2DM heritability. As a result, the impact of a particular genetic variant can be modulated by environmental factors (and vice versa) (Ge XY et al., 2013).

Pathophysiology

In terms of the disease's pathophysiology, an abnormally high blood glucose level is caused by a malfunction in the feedback loops between insulin action and insulin secretion. The body's capacity to maintain physiological glucose levels is limited when cell dysfunction results in reduced insulin secretion. On the other hand, IR causes the liver to produce more glucose and the muscle, liver, and adipose tissue to take in less glucose. Cell dysfunction is typically more severe than IR, even if both processes occur early in the pathogenesis and contribute to the development of the disease. Hyperglycemia, on the other hand, is exacerbated when both IR and -cell dysfunction are present, resulting in the progression of T2DM (Lelli D et al., 2013).

Cellular integrity must be maintained, and the physiologic mechanisms and pathways of cells must be tightly regulated, in order to maintain proper cell function. -cells are in charge of making insulin, which is made from pre-proinsulin. Proinsulin is produced when pre-proinsulin undergoes a conformational change during maturation with the assistance of several proteins in the Endoplasmic Reticulum (ER). After that, proinsulin is moved from the ER to the Golgi Apparatus (GA), where it is broken down into insulin and C-peptide in immature secretory vesicles. Insulin is stored in granules until it is released once it has matured. The primary stimulus for insulin release is an increase in glucose concentration. It's important to remember that hormones, amino acids, and other substances can also cause insulin to be released. The Glucose Transporter 2 (GLUT2), a solute carrier protein that also serves as a glucose sensor for -cells, is the primary pathway by which -cells absorb glucose when circulating glucose levels rise (Lin X-D et al., 2017).

Nutritional Factors

The circulating Very-Low-Density Lipoproteins (VLDLs), Chylomicrons (CMs), and their Remnants (CMRs), which are rich in Tri Glycerides (TG), and blood glucose are both elevated by the high-caloric Western diet. This leads to an abnormal production of inflammatory molecules and a rise in the concentration of Reactive Oxygen Species (ROS). After a substantial meal, a synergistic interaction between the two processes occurs, amplifying negative postprandial effects due to inflammation's acknowledged role as an inducer of oxidative stress. The pathogenesis of T2DM and IR is significantly influenced by the persistent and significant rise in steady-state ROS levels. As a result, mitochondrial dysfunction, ER stress, the activation of NADPH Oxidase (NOX), and the production of Superoxide (O_2) are all consequences of a pro-oxidant environment. The five major pathways that are involved in the pathogenesis of diabetes complications are activated by the increase in O_2 production: enhancement of the polyol pathway, expansion of the production of Advanced Glycation End Products (AGEs), expansion of the expression of the AGEs receptor and its activating ligands, expansion of the activating isoforms of Protein Kinase C (PKC), and expansion of the hexamine pathway's activity. In response to ischemia, increased intracellular ROS activates a number of proinflammatory pathways, causes long-lasting epigenetic changes, and drives persistent expression of proinflammatory genes even after glycaemia returns to normal through these pathways (Rihtaric D et al., 2010).

CONCLUSION

The significance of diabetes, insulin, and glucose homeostasis research has not diminished. In fact, research on this topic must continue to expand as a result of rapid globalization, the normalization of a sedentary lifestyle, and an increase in obesity, diabetes, and the co-morbidities that come with them. To prevent, control, treat, or reverse the pathophysiology of T2DM and its complications, it is essential to comprehend the mechanisms involved in each step of the disease's development and complications. Early detection of T2DM through screening and intensive patient-centered management improves quality of life for patients, but more research is needed to figure out what causes the correlations between different demographic subsets and the corresponding variable risks for T2DM, as well as what causes people with low socioeconomic status to be at higher risk. Precision medicine should be used with the help of molecular genetic tools to identify specific variants that contribute to the development of T2DM and to search for biomarkers to assess progression and response to therapeutic interventions, as the pathophysiology and underlying mechanisms of T2DM are becoming increasingly understood. To determine whether the intestinal microbiota plays a direct causal role in the pathogenesis of T2DM and how well treatments work, more research is needed (Tao Y et al., 2019) (Gouilh MA et al., 2010).

ACKNOWLEDGEMENT

None

CONFLICT OF INTEREST

None

REFERENCES

1. Boni MF, Lemey P, Jiang X, Lam TT-Y, Perry BW, et al (2020). Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. Nat Microbiol. 5: 1408-1417.
2. Latinne A, Hu B, Olival KJ, Zhu G, Zhang L, et al (2020). Origin and cross-species transmission of bat coronaviruses in China. Nat Commun. 11: 4235.
3. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF, et al (2020). The proximal origin of SARS-CoV-2. Nat Med. 26: 450-452.
4. Lau SKP, Woo PCY, Li KSM, Huang Y, Wang M, et al (2007). Complete genome sequence of bat coronavirus HKU2 from Chinese horseshoe bats revealed a much smaller spike gene with a different evolutionary lineage from the rest of the genome. Virology. 367: 428-439.
5. Ge X-Y, Li J-L, Yang X-L, Chmura AA, Zhu G, et al (2013). Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. Nature. 503: 535-538.
6. Lelli D, Papetti A, Sabelli C, Rosti E, Moreno A, et al (2013). Detection of coronaviruses in bats of various species in Italy. Viruses. 5: 2679-2689.
7. Lin X-D, Wang W, Hao Z-Y, Wang Z-X, Guo W-P, et al (2017). Extensive diversity of coronaviruses in bats from China. Virology. 507: 1-10.
8. Rihtaric D, Hostnik P, Steyer A, Grom J, Toplak I, et al (2010). Identification of SARS-like coronaviruses in horseshoe bats (Rhinolophus hipposideros) in Slovenia. Arch Virol. 155: 507-514.
9. Tao Y, Tong S (2019). Complete genome sequence of a severe acute respiratory syndrome-related coronavirus from Kenyan bats. Microbiol Resour Announc. 8: 00548-19.
10. Gouilh MA, Puechmaille SJ, Gonzalez JP, Teeling E, Kittayapong P, et al (2011). SARS-coronavirus ancestor's foot-prints in South-East Asian bat colonies and the refuge theory. Infect Genet Evol. 11: 1690-1702.