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DIABETICS AND METABOLIC FLUCTUATIONS- A MINI REVIEW

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ABSTRACT

Numerous strategies have been employed to control type 2 diabetes mellitus proficiently. In recent times, there has been a notable shift in the prevailing perspective, with increased attention being directed towards the involvement of fatty tissues in both the progression and management of the disease. Notable examples of these adipocytokines include leptin and adiponectin. The levels of adipocytokines have been found to exhibit variations in many physiological circumstances, including metabolic dysfunction, type 2 diabetes, and inflammation. Adipose tissues exhibit various characteristics, including regulating fat accumulation, energy metabolism, satiety, and insulin release. Therefore, these indicators possess the potential to offer valuable insights into the progression of metabolic dysfunction or type 2 diabetes and can be regarded as potential avenues for therapeutic interventions. The crucial functions of adipocytokines concerning satiety, appetite, control of fat storage and energy, glucose tolerance, and insulin release reinforce the involvement of fatty tissue in the progression and pathogenesis of diabetes mellitus and its associated problems.

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1. INTRODUCTION

A group of metabolic illnesses known as diabetes mellitus is characterized by the presence of persistent hyperglycemia along with varying degrees of impairment in the metabolism of proteins, lipids, and carbohydrates [1]. Diabetes mellitus can have many different causes, but they always involve either problems with the pancreas' ability to secrete insulin, problems with the body's cells' ability to react to that insulin, or problems with both at some time during the disease's progression [2,3]. Type 1 diabetes is immune-mediated or idiopathic, and type 2 diabetes accounts for most diabetes mellitus patients (non-insulin-dependent diabetes mellitus). The most prevalent kind of diabetes mellitus, type 2, is characterized by hyperglycemia, relative insulin deficiency, and impaired insulin secretion [4–7]. The projected number of persons with diabetes globally climbed from 382 million in 2013 to 422 million in 2016[6J and is anticipated to reach about 522 million by that time. In 2015, 416 million people were found to be 90% of those affected by diabetes globally have type 2 diabetes, according to statistics [8,9].

2. PHYSIOLOGICAL DIFFERENCES AND DIABETICS

Although male excess in diabetes has been observed in populations with higher type 2 diabetes, the literature claims that rates are nearly equal between men and women. This male excess in diabetes may be related to sex-related differences in insulin sensitivity due to

obesity, regional body fat deposition, and other factors like blood pressure, smoking, and alcohol consumption [10,11]. The chance of an individual dying young rises when they have diabetes. Each year, between 2012 and 2015, between 1.5 and 5.0 million fatalities were attributed to diabetes. According to World Health Organization (WHO) estimates, diabetes mellitus was the eighth greatest cause of mortality worldwide in 2012, accounting for 1.5 million deaths. Although diabetes is frequently listed as the primary cause of death certificates, another 2.2 million deaths worldwide were caused by high blood sugar and the increased risk of cardiovascular disease and other related complications (such as kidney failure). These conditions frequently result in premature death [12–14]. Although diabetes mellitus affects people everywhere, type 2 diabetes is more prevalent in developing nations. In 20-30, more persons with diabetes are anticipated in Asia and Africa. Although type 2 diabetes is frequently encountered in adults, over the past two decades, its prevalence in children has significantly increased [15–18].

3. TREATMENT ORIENTED GOALS IN DIABETICS

Men are more likely to have diabetes than women are. In developing nations, the urban population IS anticipated to quadruple between 2000 and 2030. The proportion of adults over 65 years old has increased, which is the most significant demographic trend in the prevalence of diabetes worldwide[19,20]. There are large differences between the incidence rates of various populations; incidence is highest in Finland and is lowest in Finland (0.1 per 105 each year) (37 per 105 per year). India has more people with diabetes than any other country in the world, according to statistics provided by the International Diabetes Federation (IDF) [21,22]. According to current estimates, the nation has 62 million diabetics, up from just 10 million in 2011. According to researchers, there will probably be over 100 million diabetics in India by 2030. In India, the CPR (Crude Prevalence Rate) of diabetes is estimated to be 9% in urban regions, compared to 3% in rural areas [23–25]. Impaired glucose tolerance, or IGT, is another growing issue in India. IGT is estimated to be present in urban areas at a prevalence of 8.7% and in rural regions at 7.9% [26–29]. It is estimated that 35% of people with IGT develop type 2 diabetes. In India, diabetes also starts to manifest considerably earlier in life, and chronic long-term consequences are increasing in frequency[30,31].

The major causes that contribute to the rapid spread of diabetes in India are: 1. Genetic factors - based just on genetic perspective, Indians have a four times higher risk of developing diabetes than Europeans[32,33]. The Indian diet is high in carbs and saturated fats. 2. Cultural and societal elements. This causes obesity, which then causes diabetes. Urban migration and lifestyle changes, such as adopting a sedentary lifestyle, consuming processed foods, etc [34]. Diabetes, formerly known as insulin-dependent diabetes or juvenile-onset diabetes, is caused by cell-mediated autoimmune destruction of the pancreatic beta cells, typically leading to a complete lack of insulin [35]. 85–90% of those with hyperglycemia would have one or more of the hallmarks of immunological damage to the cell, such as islet cell autoantibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase IA-2 and IA-2P [36]. The DQA and DQB genes are linked to this disease's significant HLA connections, and the DRB genes impact it. These HLA DR/DQ alleles can be protective or predisposing[37–39]. Even in the eighth and ninth decades of life, when P-cell destruction is high in children and infants but sluggish in adults, immune-mediated diabetes can develop at any age. Immune-mediated diabetes typically manifests in childhood and adolescence, although it can occur at any age. This condition is prone to ketoacidosis. The cause of this particular kind of type 1 diabetes is unknown[40]. They are impacted by ketoacidosis and have permanent insulinopenia despite showing no signs of autoimmunity. Strongly hereditary, lacking immunological proof of P-cell autoimmunity, and not HLA related, this kind of diabetes. Adult-onset diabetes, formerly known as non-insulin dependent diabetes, is characterized by individuals who have insulin resistance and a relative insulin shortage. 80% of people with diabetes have type 2 diabetes[41,42]. These people can thrive without insulin therapy. Although insulin resistance may be improved by losing weight and using medications to treat hyperglycemia, it seldom returns to normal. Type 2 diabetes has many causes, including obesity, old age, inactivity, and other factors. Ketoacidosis frequently coexists with infection. This kind of diabetes frequently remains undiagnosed for many years since the hyperglycemia develops gradually and is frequently not severe enough in the early stages for the patient to notice any of the classic indications of diabetes [43]. This leads to both microvascular and macrovascular issues. Although insulin resistance may be improved by losing weight and using medications to treat hyperglycemia, it seldom returns to

normal [44–47]. Women, those with a history of gestational diabetes, Native Americans, Blacks, and Hispanics are more likely to develop it[48].

4. PERSPECTIVES IN DIABETIC RESEARCH

The beta cells of the pancreas secrete the peptide hormone insulin. It has a molecular weight of 5.8 kDa and 51 amino acids. The first insulin synthesis stage occurs in the rough endoplasmic reticulum's ribosomes and is known as preproinsulin[49,50]. Afterward, this is broken down to proins ul in, which is then moved to the Golgi apparatus and packed into secretory granules adjacent to the cell membrane. Proinsulin is broken into equimolar quantities of insulin and C-peptide in the secretory granules. Exocytosis of insulin, C-peptide, and proinsulin occurs during insulin secretion, which also involves the fusion of secretory granules with the cell membrane [51,52]. Glucose metabolism is the primary physiological process that activates the transcription and translation of the insulin gene. Other monosaccharides, amino acids, and fatty acids, in addition to glucose, also impact insulin secretion[53,54]. The promoter regulation of the insulin gene contains many discrete sequence elements, such as A, C, E, Z, and CRE elements, which help regulate the insulin gene's expression. These elements also help to determine the location of insulin in cells. Translational processes are tightly controlled by the pancreatic ER kinase (PERK). It causes eIF2a to be phosphorylated, which controls insulin secretion. Leptin, growth hormone, GLP-1, melatonin, estrogen, and insulin secretion are regulated[55,56].

A pathological condition known as insulin resistance (IR) occurs when cells do not react to the hormone insulin as they should. Type 2 diabetes, gestational diabetes, and pre-diabetes are all primarily caused by insulin resistance. When glucose is consumed, beta cells release insulin. High blood sugar results from insulin resistance, which makes cells resistant to the hormone and unable to use it effectively. A rise in blood insulin levels is further aided by beta cells in the pancreas increasing the amount of insulin they produce[57,58]. Insulin resistance is largely influenced by obesity and a sedentary lifestyle. Other factors contributing to insulin resistance include race, particular illnesses, hormones, steroid usage, some drugs, advanced age, sleep issues, particularly sleep apnea, and tobacco use. The metabolic syndrome, a disorder linked to obesity and overweight, is the most typical insulin resistance. Type 2 diabetes and obesity are closely associated [59,60]. Obesity and type 2 diabetes are closely related conditions. Body mass index and type 2 diabetes risk and severity are tightly related (BMI).

According to Abdullah et al., obese persons have a seven times higher chance of developing diabetes than people with a healthy weight, and overweight people have a three times higher risk. Although obesity is a known risk factor for type 2 diabetes, most obese people do not develop the disease[61,62]. Body mass index (BMI) is a weight measurement concerning height frequently used to categorize adults as overweight or obese. It is calculated as the individual's kilogram weight divided by the square of their height in meters (kg/m2). The BMI is another attempt to measure how much tissue mass (muscle, fat, and bone) a person has and, based on that measurement, to classify that person as underweight, normal weight, overweight, or obese[63,64]. Compared to the European population, Asians have different associations between BMI, body fat percentage, and health risks, with a higher risk of type 2 diabetes and cardiovascular disease at BMIs below the WHO's threshold for overweight, 25 kg/m2. However, the observed risk threshold varies among Asian populations[65]. Amylin, also known as islet amyloid polypeptide (IAPP), is a peptide hormone that is co-secreted with insulin from the beta cells of the pancreas in a ratio of 100:1. Amylin and insulin are both regulated by the same stimuli since they share a regulatory promoter motif. Fatty acids and tumor necrosis factor alpha also activate the IAPP promoter[66,67]. Delaying stomach emptying and promoting satiety aids in glycemic control and inhibits an increase in postprandial blood glucose levels. Thus, it decreases both glucagon secretion and the overall demand for insulin. Proteases cut the 33 amino acid linking peptide, or C-peptide, from proinsulin. The insulin secretion rate is measured by the C-peptide[68].

5. CONCLUSION

The main purpose of measuring glycated hemoglobin (HbAlC), a kind of hemoglobin, is to determine the three-month average plasma glucose concentration. By exposing hemoglobin to plasma glucose, a non-enzymatic glycation pathway is created. HbAlc measures the beta-N-1-deoxy fructose component of hemoglobin. Glycated hemoglobin levels are higher in T2D, which implies poorer blood glucose regulation linked to cardiovascular disease, nephropathy, neuropathy, and retinopathy.

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COMPETING INTEREST

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