**Major Causes of Diabetes**

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Assignment Due Date

Diabetes is a chronic dysmetabolic syndrome defined by sustained elevated blood glucose arising from insulin insufficiency, inaction, or both. It is a worldwide healthcare burden with high morbidity and mortality rates if poorly controlled. The control of diabetes largely depends on the cause, which ranges from the interaction of genetic predisposition, environmental precipitants, insulin resistance, and other risk factors.

Genetic susceptibility majorly accounts for the aetiology of diabetes type 1. It is controlled by alleles of the genes expressing human leukocyte antigens (HLAs), i.e., HLA-DR3 and DR4 on the sixth chromosome. Moreover, monozygotic twins have a 35% proportion of diabetes type one compared to a 100% proportion for diabetes type 2 (Aitman & Todd, 1995). The interaction of a genetically susceptible person and environmental factors leads to the development of autoimmune reactions that destroy pancreatic beta-cells. Progressive destruction of beta cells between 80 and 90% causes insulin deficiency and the occurrence of classical symptoms of diabetes (Ralston et al., 2023).

The bimodal peak incidence of type 1 diabetes indicates that environmental factors contribute to the cause. These extragenetic factors trigger the destruction of beta cells by the immune system in genetically predisposed individuals. Dietary contact to dairy products during infancy, viral infections from mumps, rubella, enterovirus, cytomegalovirus, and Epstein-Barr virus have been implicated. Cow’s milk has antigens like islet cell antigen, i.e., bovine serum albumin, whereas viral infections initiate and modify autoimmunity, resulting in beta cell destruction and developing diabetes in later life (Ralston et al., 2023 & Skoglund, 2011).

 People suffering from other autoimmune conditions, such as Hashimoto thyroiditis, have a higher prevalence of type 1 diabetes (Pilia et al., 2011). Dietary toxins, such as nitrosamines, majorly found in coffee, cured, and smoked meats, have been proposed as potential diabetogenic toxins. Limited childhood exposure to microbes causing upper respiratory tract infections, especially in the first 6 months of life, reduced the risk for type 1 diabetes due to lowered islet autoantibody seroconversion (Khardori, 2023).

A relative insulin deficiency, often brought up resistance to the actions of insulin, followed by impaired pancreatic beta cell function, largely causes type 2 diabetes. This resistance to insulin is attributed to central obesity and non-alcoholic fatty liver disease, which increase free fatty acids and glycerol, allowing for gluconeogenesis that results in hyperglycaemia. Obese, genetically predisposed people had a tenfold risk of developing type 2 diabetes, as obesity acts as a diabetogenic factor to insulin resistance and beta-cell impairment (Ralston et al., 2023).

 Sedentarism, inactivity, and overeating down-regulate insulin sensitivity, increase pancreatic beta-cell demand to secrete insulin, and allow for the accumulation of free fatty acids in skeletal muscles. The development of diabetes type 2 was primarily in mid-adulthood and older people; however, it has been noted with increasing frequency in young individuals. The increased incidence of diabetes type 2 is largely present along with racial and ethnic susceptibility and the obese prepubertal children, teenagers, and young adults (Albert et al., 2004).

 Ethnical and tribal contrasts have been observed in the prevalence of diabetes type 2, with African Americans, Native Americans, Asians, and Hispanics being more susceptible than non-Hispanic groups (Khardori, 2023).

Chronic metabolic syndrome, often characterized by endocrine dysfunction such as dyslipidaemia, polycystic ovarian syndrome (in women), high blood pressure, visceral obesity, and non-alcoholic fatty liver disease, results in multiple defects in insulin signalling leading to progression from normal to abnormal glucose tolerance and induction of insulin resistance. Typically, individuals with metabolic derangements develop type 2 diabetes in later life (Ralston et al., 2023).

 The history of developing gestational diabetes or macrosomia babies puts people at risk of developing diabetes. Gestational diabetes, a pregnancy complication, occurs when the decreased maternal sensitivity cannot be counteracted by sufficient maternal insulin secretion. Failure of resolution of insulin sensitivity during pregnancy leads to delivery of babies with a birth weight of over 9 lb or the development of maternal diabetes postpartum (Khardori, 2023).

A familial history of type 2 diabetes with or without a genetic susceptibility is attributed to developing type 2 diabetes. First-degree relatives, such as parents or siblings with autosomal dominant genetic predisposition causing dysfunction in beta-cells; also called maturity-onset diabetes of youth (MODY), account for diabetes type 2 at a young age (Cefalu, 2000).

Medications taken for treatment or management of other diseases have been implicated to promote weight gain, depressive states, and alter glucose homeostasis. These medications range from antidepressants such as phenytoin; hormonal pills such as estrogens; steroids such as glucocorticoids; and antihypertensives such as thiazides. The long-term use of these medications produces undesirable effects that encourage the development of type 2 diabetes (Ralston et al., 2023).

Other intercurrent endocrine dysfunction attributed to other endocrine diseases such as acromegaly, pheochromocytoma, Cushing syndrome, and thyrotoxicosis have been identified as potential causes of diabetes. These diseases result in excess endogenous secretion of insulin antagonists such as cortisol, growth hormone, thyroid hormones, and catecholamines. This increased secretion of these stress hormones precipitates hyperglycaemia and dehydration (Ralston et al., 2023).

The causes of diabetes are multifactorial in both types 1 and 2, ranging from the interaction of genetic predisposition, environmental triggers, insulin insensitivity, and modifiable and non-modifiable risk factors.

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