International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

A Review on Diabetes Mellitus

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Submitted: 08-12-2022 Accepted: 17-12-2022

ABSTRACT: This article's goal is to review data about diabetes mellitus. A chronic hyperglycaemic state brought on by abnormalities in insulin secretion, action, or both defines diabetes mellitus (DM), a group of metabolic diseases. While a combination of environmental variables including obesity, overeating, and lack of exercise, as well as genetic factors associated to decreased insulin production and insulin resistance, cause type 2 diabetes, stress, and ageing, type 1 diabetes is the result of an autoimmune reaction to proteins of the islets cells of the pancreas. The metabolic problems associated with type 1 diabetes are caused by a decrease in insulin secretion or autoimmune destruction of pancreatic cells. The main pathophysiological features of type 2 diabetes are decreased insulin production and increased insulin resistance. Although ageing, obesity, insufficient energy intake, alcohol consumption, smoking, etc. are important risk factors in the development of type 2 diabetes mellitus; however, the reduction in pancreatic cell function clearly shows progression through time.

Key words: Diabetes mellitus, Pathogenesis, Pathophysiology, Etiology, Signandsymptoms, Risk Factors, Screening and Diagnosis, Treatment.

I. INTRODUCTION

Diabetes mellitus is a long-term condition of the metabolism of proteins, lipids, and carbohydrates. Hyperglycemia is a symptom shared by a number of metabolic illnesses, including diabetes mellitus. Diabetes-related hyperglycemia is caused by deficiencies in either insulin action, secretion, or—more frequently—both. The metabolic dysregulation brought on by the chronic hyperglycemia, particularly in the kidneys, eyes, nerves, and blood vessels, may be linked to secondary damage in a variety of organ systems. Diabetes mellitus is a collection of diverse illnesses that frequently manifest with bouts of hyperglycemia and glucose intolerance due to a deficiency in insulin, a problem with the way that insulin works, or both. The most prevalent endocrine condition, which is sometimes referred to as "sugar," is one in which there is insufficient or no insulin present or, less frequently, impaired insulin activity (insulin resistance).

Both the hormones glucagon and insulin are secreted by the pancreas. Insulin and glucagon are both secreted by the beta (ß) and alpha (α) cells in the islets of Langerhans. Insulin decreases blood sugar levels by promoting glycogenesis and supplying glucose to the muscles, liver, and adipose tissue. While alpha (α) cells play a significant role in managing blood glucose by generating glucagon, which raises blood glucose levels by accelerating glycogenolysis, erythrocytes and neural tissue do not require insulin to utilize glucose. More than 8% of the population, or more than 25 million children and adults, in the United States have diabetes, with about a third of them currently being completely uninformed

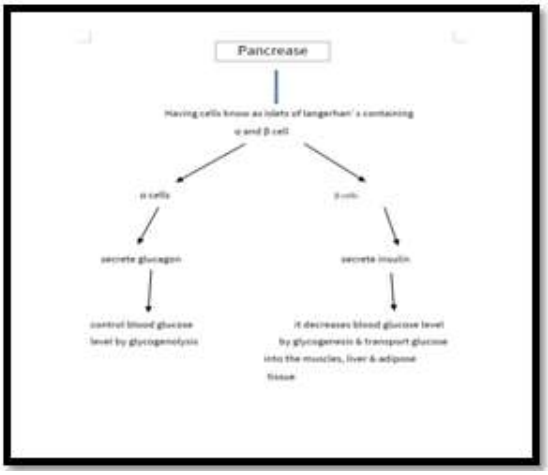

Fig: represent flow chart of secretion of insulin and glucagon

that they have hyperglycemia, according to the American Diabetes Association. Each year, the United States sees the diagnosis of over 1.9 million new cases of adult diabetes.

II. HISTORY

The Greek word "diabetes" means "to pass through," and the Latin word "Mellitus" means "sweet" together make up the word "diabetes

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

mellitus." In 230 BCE, the Greek Apollonius of Memphis coined the phrase "diabetes" or "to pass through." One of the first diseases to be named was diabetes, which was described as having a "very considerable emptying of the urine" in an Egyptian document from 1500 BCE. Type 1 diabetes is thought to have been present in the first cases described. Around the same time, Indian doctors diagnosed the condition and labeled it as madhumeha, or "honey urine," noticing that the urine would draw ants. The Indian doctors Sushruta and Charaka initially distinguished two forms of diabetes as distinct diseases in 400–500 BCE.

III. IN INDIA

The prevalence of diabetes has been rising gradually in India since 1990 and rapidly since the year 2000. According to the IDF, India has seen an increase in the prevalence of diabetes during the previous ten years. The prevalence of diabetes increased in India from 7.1% in 2009 to 8.9% in 2019. IGT is thought to affect 25.2 million persons currently, and 35.7 million adults are thought to have it by 2045. In the world's diabetes epidemic, India is in second place to China with 77 million diabetics. 12.1 million of them, or 27.5 million by the year 2045, are predicted to be older than 65.According to statistics gathered from cross-sectional surveys carried out across the nation, diabetes is growing more common in India. Based on a urine analysis, the first study, which included 18,243 participants, indicated that the prevalence of diabetes was 1.5%. Several national studies on the prevalence of diabetes have been conducted.The multicenter ICMR survey, carried out between 1972 and 1975 in Ahmedabad, Calcutta, Cuttack, Delhi, Poona, and Trivandrum, as well as nearby rural areas, revealed a nationwide prevalence of diabetes of 2.1%. The Prevalence of Diabetes in India Study, conducted in 40 urban and 37 small towns and rural areas throughout India in 2004, found that the prevalence of diabetes was 5.9 and 2.7%, respectively. According to the age-standardized prevalence recorded by the National Urban Diabetes Survey, which was carried out in India's six largest cities in 2001, the disease affects 12.1% of the population. Self-reported diabetes prevalence was 4.5% according to the WHO ICMR NCD Risk Factor Surveillance Study, which was carried out between 2003 and 2005 in urban and rural areas of six distinct states.

IV. CLASSIFICATION

The classification now in use is based on the pathogenesis and etiology of the disease and is helpful in determining the necessary therapy and clinical assessment of the disease.

- Type 1 diabetes mellitus (T1DM),
- Type 2 diabetes mellitus (T2DM),
- Gestational diabetes mellitus (GDM), and
- Diabetes induced or related with certain specific illnesses According to these classification, these are the four primary forms or categories of diabetes, respectively.

V. PATHOGENESIS

The following explanation explains the pathogenesis of diabetes mellitus:

Type 1 diabetes mellitus pathogenesis:

The primary feature of type 1 diabetes is the breakdown of beta-cell mass, which typically results in a complete lack of insulin. Three mutually interconnected pathways are used to explain the pathogenesis of type 1 diabetes mellitus is:

- **Genetic vulnerability:** The inheritance of several genes contributes to the vulnerability to type 1 diabetes mellitus:If one identical twin has type 1 diabetes mellitus, there is an approximately 50% probability that the other will also have it, although not always. This indicates that in these circumstances, additional moderating factors play a role in the development of diabetes mellitus.
- **Autoimmune factors:** Numerous immunologic abnormalities have been identified in studies on humans and animal models of type 1 diabetes mellitus. Selective elimination of beta -cells while leaving undamaged other islet cell types, such as PP cells or alpha cells that produce polypeptides or glucagon. Apoptosis or T-cell mediated cytotoxicity are the mechanisms involved in this.
- **Environmental variables:** Even while no one of these environmental factors has been definitively proven to have a part in the etiology of type 1 diabetes mellitus, epidemiologic studies do suggest their significance. In fact, the trigger might come on years before the disease manifests itself. It appears that certain dietary and viral proteins have antigenic qualities in common with human cell surface proteins, and that this molecular mimicry is what causes the immune system to target -cells.

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Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

Type 2 Diabetes mellitus pathogenesis:

In type 2 diabetes mellitus, the primary metabolic abnormality is either reduced insulin secretion—a delayed insulin response to glucose load—or peripheral tissue insensitivity to insulin. Although type 2 diabetes mellitus is far more frequent than type 1 and has a more complex etiology, little is known about its pathophysiology. Although a number of reasons have been suggested, autoimmune symptoms and HLA connection have not been mentioned.

VI. PATHOPHYSIOLOGY

Type 1 diabetes mellitus:

Previously known as diabetes that is prone to ketosis or juvenile onset. Other autoimmune diseases like Graves' disease, Hashimoto's thyroiditis, and Addison's disease may also be sought after [5].

Insulin-dependent diabetes mellitus (IDDM), often known as type I diabetes, primarily affects children and young adults. Its onset is typically abrupt and can be fatal [4].

In Type 1 Diabetes, CD4+ and CD8+ T lymphocytes and invading macrophages attack insulin-producing cells in the pancreas, causing autoimmunity [3]. The metabolic abnormalities associated with T1DM are caused by a lack of insulin production, which is caused by the autoimmune death of pancreatic beta-cells.

Insulin is not produced by those with type 1. Adipose and muscle cells cannot obtain glucose to meet their energy needs without insulin. When muscle and adipose tissues are starved of glucose, an excess of glucagon is released, which triggers glycogenolysis and gluconeogenesis. In healthy people, hyperglycemia reduces glucagon secretion; however, in those with T1DM, hyperglycemia has no effect on glucagon secretion [2]. The metabolic abnormalities brought on by insulin insufficiency are made worse by the consequent unnecessarily increased glucagon levels. Blood glucose levels increase. The ever-increasing glucose cannot be absorbed by the kidneys, therefore the excess is eliminated in the urine (polyuria). Due to this fluid loss, the brain communicates hunger and thirst (polydipsia) (polyphagia). If this process continues, the liver will digest stored lipids and turn them into keto acids.This induces acidosis and lower pH levels.

In addition to the typical immune-mediated destruction of pancreatic beta-cells, patients with T1DM have been identified to have a higher incidence of a number of many other autoimmune diseases, such as myasthenia gravis, Addison's disease (primary adrenal insufficiency), celiac sprue (celiac disease), pernicious anemia, vitiligo, Hashimoto's thyroiditis, Graves' disease, dermatomyo [10,16,17,18].

Type 2 diabetes mellitus:

T2DM, sometimes referred to as adult-onset diabetes or non-insulin-dependent diabetes mellitus (NIDDM).

Insulin resistance and -cell dysfunction are two primary insulin-related anomalies that reveal this form of diabetes.

Contrary to T1DM, no association in between illness and genetics associated in the immune response, including autoimmunity, has been discovered, and as a result, there is no immune-mediated pancreatic -cell death. [23,24]

Patients with T2DM frequently do not need insulin therapy at the time of illness start or even subsequently, throughout their lives, if there are no significant physiological stress situations. (19,20,21)

Growing older, being obese, having a family history of diabetes, being physically inactive, and adopting modern lifestyles have all been linked to T2DM more commonly. When the pancreatic beta cells are unable to produce enough insulin to meet metabolic requirements, type 2

These kinds of diabetes are caused by diabetes develops.

Additionally, Type 2 diabetes develops a notable trait of insulin resistance as adipose cells are formed in the patient's liver and muscle. As a result, type 2 diabetes is more prevalent among people with more adipose deposition, who often have higher body fat percentages and obese BMIs.

Patients with T2DM typically encounter numerous cardiovascular risk factors, such as hypertension and lipoprotein metabolic abnormalities characterized by raised triglycerides and decreased numbers of high-density lipoproteins, due to its strong association with increased body fat content or obesity (HDLs).

Gestational diabetes mellitus:

The terminology "gestational diabetes mellitus" refers to any undetected type 2 diabetes, along with any degree of glucose intolerance or diabetes, which may occur during or prior to the time of conception. (10,26)

The blood glucose levels rise during the third trimester of pregnancy and are referred to as gestational diabetes mellitus (GDM) when they reach diabetic levels. During early pregnancy, both the fasting and post-prandial blood glucose levels

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

are typically lower than normal. (27,28) Age, obesity, previous pregnancies that resulted in large babies, and any prior history of poor glucose tolerance or GDM all enhance the chance of developing GDM. [29,30] Additionally, GDM has been linked to a higher lifetime risk of getting T2DM.

Other types diabetes:

Genetic anomalies in insulin action, endocrinopathies, exocrine pancreatic diseases, monogenic deficiencies in -cell activity, and a number of other distinct illnesses. abnormalities in -cell function that are monogenic and result in diabetes Only 0.6–2% of all occurrences of diabetes are caused by monogenic abnormalities in -cell function, which mostly include neonatal diabetes and maturity-onset diabetes of the young (MODY), which are the rarest types of diabetes.

VII. ETIOLOGY

The Greek term "aetiologia" is the source of the word "etiology." Therefore, etiology is defined as the science of determining the causes and origins of a disease. The causes of diabetes mellitus include the following:

Genetic defects of B-cell function, Mutations in mitochondrial DNA, and genetic defects in insulin action are examples of genetic factors that may contribute to diabetes mellitus (DM).

Environmental factors include: obesity linked to rising living standards, steady urban migration,changes in lifestyle (including alcohol consumption), and lack of physical activity brought on by sedentary lifestyle.

Internal factors: These include: Autoantibody production that kills ßcells in the pancreas; Insufficiency in insulin synthesis and secretion; and Insulin sensitivity (because the cells do not respond to the insulin produced),the existence of conditions that can severely harm the pancreas, including those that cause trauma, infection, pancreatic cancer, and pancreatectomy. Excess hormone secretion that interferes with insulin action (e.g., growth hormone, cortisol, glucagon, epinephrine), Drug-induced impairment of insulin secretion, and Viral infections that result in B-cell death.

VIII. SIGN AND SYMPTOMS

Type 1 diabetes mellitus:

Type 1 diabetics may also experience nausea, vomiting, or stomach discomfort. The signs and symptoms of type 1 diabetes can become severe in as little as a few weeks or months. Although it can being at any age, type 1 diabetes typically manifests in children, teenagers, or young adult.

Type 2 diabetes mellitus:

It can take years for type 2 diabetes symptoms to manifest. Some people seldom ever experience any symptoms. Despite the fact that type 2 diabetes affects children and teenagers more frequently, it typically strikes adults first. Because the symptoms of type 2 diabetes are subtle, understanding the risk factors is essential. Ensure that if you experience any of them, you see your doctor.

IX. RISK FACTORS

Type 1 diabetes mellitus:

- Having a parent or sibling with type 1 diabetes in the family.
- Damage to the pancreas (such as by infection, tumor, surgery or accident).
- Autoantibodies, or antibodies that erroneously target your own body's tissues or organs, are present.
- Tension (such as surgery or illness).
- Exposure to virus-based diseases.

Prediabetes or Type 2 diabetes mellitus:

- Belonging to the Black, Hispanic, Native American, Asian American, or Pacific Islander races and ethnicities.
- Being obese or overweight.
- Blood pressure is high.
- Having low levels of HDL cholesterol (the "good" cholesterol) and high triglyceride levels.
- Being 45 or older .
- Lack of physical activity,
- Gestational diabetes, or giving birth to a child who weighs more than 9 pounds are all risk factors.
- Being affected by polycystic ovarian syndrome.
- Having had a heart attack or a stroke in the past.
- Having smoked.

X. SCREENING AND DIAGNOSIS

Although postprandial blood sugar, random blood sugar, and glucose tolerance tests are also used for blood sugar measurement, the American Diabetes Association (ADA) recommends using the fasting glucose concentration for regular diabetes screening. The 1997 ADA criteria for diagnosing DM place a greater emphasis on the FPG (Fasting Plasma

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

Glucose) than the OGTT (Oral Glucose Tolerance Test). Fructosamine and glycated hemoglobin (HbA1c) are still useful for assessing blood sugar control over time. Normal blood glucose levels are kept within a fairly specific range of 70 to 120 mg/dL. The ADA and WHO list the following as diagnostic criteria for diabetes:

- ≥126 mg/dL for fasting plasma glucose, ≥200 mg/dL for random plasma glucose, in a patient with classic hyperglycemic sign
- ≥200 mg/dL for 2-hour plasma glucose during an oral glucose tolerance test (OGTT) with a loading dose of 75 gm.
- a HbA1C (glycated hemoglobin) reading ≥6.5%.

Test for type 1 and type 2 diabetes mellitus:

- **Glycated hemoglobin (A1C) test:** It reveals your average blood sugar level over the previous two to three months without requiring you too fast. It determines how much of the protein haemoglobin, which carries oxygen in red blood cells, is bound to blood sugar. The more hemoglobin with sugar linked you have, the higher your blood sugar levels will be. You have diabetes if your A1C result is 6.5% or above on two different tests. If your A1C ranges between 5.7% and 6.4%, you have prediabetes. 5.7% or less is regarded as usual.
- **Fasting blood sugar test:** After you haven't eaten anything the previous night, a blood sample will be taken (fast). Normal fasting blood sugar ranges are fewer than 100 mg/dL (5.6 mmol/L). Prediabetes is defined as fasting blood sugar levels of 5.6 to 6.9 mmol/L or above, or 100 to 125 mg/dL. You have diabetes if your level on two different tests is 126 mg/dL (7 mmol/L) or above.
- **Oral glucose tolerance test :** You must fast the night before this test. The blood sugar level before fasting is then determined. Every two hours after having a sweet beverage, blood sugar levels are measured. Blood sugar levels under 140 mg/dL (7.8 mmol/L) are considered normal. After two hours, a result of greater than 200 mg/dL (11.1 mmol/L) indicates diabetes. If your blood sugar level is between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L), you have prediabetes.
- **Random blood sugar test :** At some random time, a blood sample will be obtained. A blood sugar level of 200 mg/dL (11.1 mmol/L) or greater is considered to be diabetic regardless of when you last had food**.**

XI. TREATMENT

A combination of lifestyle modifications and drug therapy is required for diabetic patients in order to achieve and maintain long-term good metabolic control. Various medications, both oral and injectable, are currently available to treat diabetes mellitus (DM). The necessity for effective glycogenic management is determined by treatment guidelines that aim to stop the progression or emergence of diabetes problems.

Lack of insulin is the primary cause of type 1 diabetes mellitus. Insulin should be administered intravenously to Type 1 patients.

Insulin resistance in cells is the primary cause of type 2 diabetes mellitus. The most typical type of diabetes can be treated with:

- The substance that causes the pancreas to produce more insulin,
- The substance that makes the target organ more sensitive to insulin, and
- The substance that slows down the absorption of glucose from the gastrointestinal tract.

Treatment for type 1 diabetes mellitus:

The type 1 diabetes treatment strategy entails taking insulin, keeping track of calories and macronutrients, and monitoring blood sugar levels. eating nutritious food. Periodic exercise activity and having a healthy weight.

Treatment for type 2 diabetes mellitus:

Healthy nutrition, regular exercise, weight loss, and maybe diabetes medication or insulin therapy are all part of the type 2 diabetes treatment strategy. Checking blood sugar levels. To maintain the blood sugar level as closely as possible to normal. The target range for daytime blood sugar levels before meals is typically 80–130 mg/dl (4.44–7.2 mol/L). Two hours after a meal, blood sugar levels shouldn't be greater than 180 mg/dl (10 mol/L).

Insulin injection

When oral medication does not manage blood sugar levels in patients with type 1 or type 2 diabetes, insulin injections are administered.

- **Short-acting insulin :**This type of insulin, often known as normal insulin, begins to function about 30 minutes after injection. It lasts for around 4 to 6 hours, reaching its full effect at 90 to 120 minutes.
- **Rapid-acting insulin:** This kind of insulin begins to function within 15 minutes. It has a peak effect after 60 minutes and lasts around 4

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

hours. This kind is frequently taken 15 to 20 minutes prior to meals.

- **Intermediate-acting insulin:** This form of insulin, also known as NPH insulin, begins to operate within one to three hours. It has its full effect between 6 and 8 hours into its 12- to 24-hour duration.
- **Long and Ultra-long acting insulin:** This kind of insulin may offer protection for up to 14 to 40 hours.

Oral hypoglycemic agent

By lowering blood glucose levels, hypoglycemic agents are used to treat diabetes mellitus. All other hypoglycaemic medications, with the exception of insulin, exenatide, liraglutide, and pramlinited, are administered orally and are referred to as oral hypoglycemic medications or oral antihyperglycemic medications. Examples.

- Sulfonylurea's(Tolbutamide, chlorpropamide, Glibenclamide (Glyburide), Glipizide, Gliclazide, Glimepride).
- Biguanides (Phenformin Metformin Meglitinide Analogues Repaglinide Nateglinide).
- Thiazolidinediones (Rosiglitazone Pioglitazone)
- α Glucosidase inhibitors (Acarbose Miglitol).

XII. CONCLUSION

Above article is about diabetes mellitus, how diabetes comes into the world and what side effects they have and their treatment. Which gives some ideas regarding how disturbance in blood sugar level causes diabetes in the body. This article we studied information about introduction, pathophysiology, etiology, risk factor, complications, in detail regarding diabetes mellitus. It's a very serious complication in life . Lifestyle and Daily routine of day to day circumstances play a greater role in occurring this type of serious complications. Diabetes is a costly disease affecting the developing global economic level and increases worldwidely upto 400 million people. This article has an update on benefits of different drugs used for the treatment of diabetes mellitus for both current and future. Above article contains ideas about type 1 and type 2 diabetes mellitus. Type 1 diabetes mellitus is insulin dependent diabetes mellitus and type 2 is non dependent insulin diabetes mellitus].

REFERENCE

[1]. (Bruno, Merletti, 1990, reviewed 2017).

[2]. Holt RI (2004) Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. Br J Psychiatry Suppl 47: S55-63.

[3]. Al Homsi MF, Lukic ML (1992) An Update on the pathogenesis of Diabetes Mellitus, Department of Pathology and Medical Microbiology (Immunology Unit) Faculty of Medicine and Health Sciences, UAE University, Al Ain, United Arab Emirates.

[4]. Wassmuth R, Lernmark A. The genetics of susceptibility to diabetes, ClinImmunol, Immunopathol. 1989; 53:358399,

[5]. Jun SK, Yoon YW. A new look at viruses in Type 1 diabetes, Diabetes/Metabolism Research and Reviews. 2002; 19:8-31.

[6]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar.

[7]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. American Diabetes Association. Microvascular complications and foot care: Standards of medical care in diabetes—2018. Diabetes Care. 2018;41:S105–

[8]. [PubMed] [Google Scholar] 8. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. American Diabetes Association Cardiovascular disease and risk management: Standards of medical care in diabetes—2018. Diabetes Care. 2018;41:S86–104. [PubMed] [Google Scholar]

[9]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. Rawshani A, Rawshani A, Franzén S, Eliasson B, Svensson AM, Miftaraj M, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. N Engl J Med. 2017;376:1407-18 [PubMed] [Google Scholar]

[10]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37:S81–90. [PubMed] [Google Scholar]

[11]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. American Diabetes Association. Introduction: Standards of medical care in diabetes—2018. Diabetes Care. 2018;41:S1–2. [PubMed] [Google Scholar]

[12]. Mujeeb Z. Banday, Aga S. Sameer, and Saniya Nissar. Blas E, Kuru A, editors. Equity, Social Determinants and Public

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1373-1380 www.ijprajournal.com ISSN: 2456-4494

Health Programmes. Geneva, Switzerland: World Health Organization; 2010. Diabetes: Equity and social determinants. [Google Scholar]

[13]. American Diabetes Association. Classification and diagnosis of diabetes: Standards of medical care in diabetes—2018. Diabetes Care. 2018;41:S13–27. [PubMed] [Google Scholar]

[14]. Taplin CE, Barker JM. Autoantibodies in type 1 diabetes. Autoimmunity. 2008;41:11–8. [PubMed] [Google Scholar]

[15]. Lahtela JT, Knip M, Paul R, Antonen J, Salmi J. Severe antibody-mediated human insulin resistance: Successful treatment with the insulin analog lispro. A case report. Diabetes Care. 1997;20:71–3. [PubMed] [Google Scholar]

[16]. Knip M, Siljander H. Autoimmune mechanisms in type 1 diabetes. Autoimmun Rev. 2008;7:550–7. [PubMed] [Google Scholar]

[17]. Hughes JW, Riddlesworth TD, DiMeglio LA, Miller KM, Rickels MR, McGill JB T1D Exchange Clinic Network. Autoimmune diseases in children and adults with type 1 diabetes from the T1D exchange clinic registry. J Clin Endocrinol Metab. 2016;101:4931–7. [PMC free article] [PubMed] [Google Scholar]

[18]. Triolo TM, Armstrong TK, McFann K, Yu L, Rewers MJ, Klingensmith GJ, et al. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. Diabetes Care. 2011;34:1211–3. [PMC free article] [PubMed] [Google Scholar]

[19]. Leahy JL. Pathogenesis of type 2 diabetes mellitus. Arch Med Res. 2005;36:197–209. [PubMed] [Google Scholar]

[20]. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am. 2004;88:787–835, ix. [PubMed] [Google Scholar]

[21]. Muoio DM, Newgard CB. Mechanisms of disease:molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. Nat Rev Mol Cell Biol. 2008;9:193–205. [PubMed] [Google Scholar]

[22]. Jaiswal N, Gavin MG, Quinn WJ, Luongo TS, Gelfer RG, Baur JA, Titchenell PM. The role of skeletal muscle Akt in the regulation of muscle mass and glucose homeostasis. Mol Metab. 2019 Oct;28:1-13. [PMC free article] [PubMed] [Ref list]

[23]. Frayling TM. Genome-wide association studies provide new insights into type 2 diabetes aetiology. Nat Rev Genet. 2007;8:657–62. [PubMed] [Google Scholar]

[24]. Zeggini E, Scott LJ, Saxena R, Voight BF, Marchini JL, Hu T, et al. Wellcome Trust Case Control Consortium. Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. Nat Genet. 2008;40:638–45. [PMC free article] [PubMed] [Google Scholar]

[25]. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444:840–6. [PubMed] [Google Scholar]

[26]. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999–2005. Diabetes Care. 2008;31:899–904. [PubMed] [Google Scholar]

[27]. Yuen L, Wong VW. Gestational diabetes mellitus: Challenges for different ethnic groups. World J Diabetes. 2015;6:1024–32. [PMC free article] [PubMed] [Google Scholar]

[28]. Hedderson MM, Darbinian JA, Ferrara A. Disparities in the risk of gestational diabetes by race-ethnicity and country of birth. Paediatr Perinat Epidemiol. 2010;24:441–8. [PMC free article] [PubMed] [Google Scholar]

[29]. Cosson E. Diagnostic criteria for gestational diabetes mellitus. Diabetes Metab. 2010;36:538–48. [PubMed] [Google Scholar]

[30]. Kim C. Gestational diabetes: Risks, management, and treatment options. Int J Womens Health. 2010;2:339–51. [PMC free article] [PubMed] [Google Scholar]

[31]. Noctor E, Crowe C, Carmody LA, Saunders JA, Kirwan B, O'Dea A, et al. ATLANTIC-DIP Investigators. Abnormal glucose tolerance post-gestational diabetes mellitus as defined by the international association of diabetes and pregnancy study groups criteria. Eur J Endocrinol.

2016;175:287–97. [PubMed] [Google Scholar]

[32]. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: A systematic review. Diabetes Care. 2002;25:1862–8. [PubMed] [Google Scholar]

[33]. Aroda VR, Christophi CA, Edelstein SL, Zhang P, Herman WH, Barrett-Connor E, et al. Diabetes Prevention Program Research Group. The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: The Diabetes Prevention Program outcomes study 10-year follow-up. J Clin Endocrinol Metab. 2015;100:1646–53. [PMC free article] [PubMed] [Google Scholar]

[34]. Gardner DS, Tai ES. Clinical features and treatment of maturity onset diabetes of the young [MODY] Diabetes Metab Syndr Obes. 2012;5:101–8. [PMC free article] [PubMed] [Google Scholar]

[35]. Shields BM, Hicks S, Shepherd MH, Colclough K, Hattersley AT, Ellard S. Maturity-onset diabetes of the young (MODY): How many cases are we missing? Diabetologia. 2010;53:2504–8. [PubMed] [Google Scholar]

[36]. Kim SH. Maturity-onset diabetes of the young: What do clinicians need to know? Diabetes Metab J. 2015;39:468–77. [PMC free article] [PubMed] [Google Scholar]

[37]. Vaxillaire M, Froguel P. Monogenic diabetes in the young, pharmacogenetics and relevance to multifactorial forms of type 2 diabetes. Endocr Rev. 2008;29:254–64. [PubMed] [Google Scholar]

[38]. Froguel P, Velho G. Molecular genetics of maturity-onset diabetes of the young. Trends Endocrinol Metab. 1999;10:142–6. [PubMed] [Google Scholar]

[39]. Iafusco D, Massa O, Pasquino B, Colombo C, Iughetti L, Bizzarri C, et al. Early Diabetes Study Group of ISPED. Minimal incidence of neonatal/infancy onset diabetes in Italy is 1:90,000 live births. Acta Diabetol. 2012;49:405–8. [PMC free article] [PubMed] [Google Scholar]

[40]. Polak M, Cavé H. Neonatal diabetes mellitus: A disease linked to multiple mechanisms. Orphanet J Rare Dis. 2007;2:12. [PMC free article] [PubMed] [Google Scholar]

[41]. Aguilar-Bryan L, Bryan J. Neonatal diabetes mellitus. Endocr Rev. 2008;29:265–91. [PMC free article] [Pub Med] [Google Scholar].