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A Review on Diabetes Mellitus its Types, Pathophysiology, Epidermiology and its Global Burden

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ABSTRACT

The spread of obesity and unhealthy lifestyles has contributed to a significant and increasing disease burden associated with diabetes in all countries worldwide. According to recent estimates, the worldwide prevalence of diabetes in 2013 was recorded at 382 million individuals, with projections indicating a significant increase to 592 million by the year 2035. The categorization of diabetes based on its aetiology has gained widespread acceptance in the scientific community. There are two primary classifications of diabetes, namely type 1 and type 2. Type 2 diabetes is the predominant kind, constituting a majority proportion (>85%) of the overall prevalence of diabetes. Both types of diabetes have the potential to result in a range of problems affecting several bodily systems. These complications can manifest as microvascular endpoints such as retinopathy, nephropathy, and neuropathy, as well as macrovascular endpoints including ischemic heart disease, stroke, and peripheral vascular disease. Diabetes is a significant public health concern because to its association with premature morbidity, death, diminished life expectancy, and substantial financial and societal burdens. Diabetes mellitus is a chronic metabolic illness characterised by heterogeneity and a complex pathophysiology. The condition is distinguished by increased amounts of glucose in the bloodstream, known as hyperglycemia, which arises from irregularities in either the production of insulin or the effectiveness of insulin, or both. Traditionally, diabetes has been classified into three distinct types: Type 1 DM, also known as insulin-dependent diabetes mellitus (IDDM), characterised by the body's inability to make insulin, necessitating the administration of insulin by injections or the use of an insulin pump. This condition is commonly referred to as "juvenile diabetes" in medical literature. Type 2 diabetes mellitus, also known as non-insulin dependent diabetes mellitus (NIDDM), arises due to the presence of insulin resistance. This condition occurs when cells are unable to effectively utilise insulin, either with or without a complete absence of insulin. This particular classification was once denoted as "adult-onset diabetes". The third primary category is gestational diabetes, which manifests when women who do not have a prior medical history of diabetes experience elevated levels of blood glucose throughout their pregnancy. It is plausible that it may occur prior to the onset of type 2 diabetes mellitus. This article explores the various forms, pathophysiology, epidemiology, and global burden associated with the topic under discussion.

Keywords- Diabetes mellitus, Pathophysiology, Type I diabetes, Type II diabetes.

I. INTRODUCTION

Diabetes mellitus encompasses a diverse range of conditions that are distinguished by elevated blood glucose levels resulting from either an insufficient generation of insulin or a diminished response to its effects[1]. Diabetes mellitus is characterised by persistent hyperglycemia, which has been linked to the development of end organ damage, malfunction, and failure in various bodily systems, such as the retina, kidney, neurological system, heart, and blood vessels. According to the International Diabetes Federation

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(IDF), the global prevalence of diabetes mellitus was estimated to be 366 million in 2011, with a projected increase to 552 million by the year 2030[2].

Diabetes mellitus (DM) is the most prevalent endocrine illness, impacting over 100 million individuals globally, which accounts for around 6% of the global population. The condition is attributed to a lack or inadequate production of insulin by the pancreas, leading to alterations in the levels of glucose in the bloodstream[3]. It has been observed to have detrimental effects on various bodily systems, specifically the blood vessels, eyes, kidneys, heart, and nerves. Diabetes mellitus has been categorised into two distinct types: insulin dependent diabetes mellitus (IDDM, Type I) and non-insulin dependent diabetes mellitus (NIDDM, Type II). Type I diabetes is classified as an autoimmune disorder, distinguished by a localised inflammatory response occurring within and surrounding islets, subsequently leading to the targeted elimination of cells responsible for insulin secretion[4].

In contrast, Type II diabetes is characterised by peripheral insulin resistance and compromised insulin secretion. The existence of diabetes mellitus (DM) is associated with an elevated risk of several consequences, including cardiovascular illnesses, peripheral vascular disorders, stroke, neuropathy, renal failure, retinopathy, blindness, and amputations, among others. Pharmaceutical substances are primarily employed with the purpose of preserving life and mitigating symptoms. The secondary objectives of this study are to mitigate the occurrence of chronic problems associated with diabetes and to enhance overall lifespan by mitigating numerous risk variables[5]. Insulin replacement therapy is widely regarded as the primary therapeutic approach for individuals diagnosed with type 1 diabetes mellitus, whereas dietary and lifestyle adjustments are recognised as fundamental components in the treatment and overall management of type 2 diabetes mellitus. There are several classes of hypoglycemic medications, including biguanides and sulfonylureas, that are utilised in the management of diabetes[6].

However, it should be noted that none of these treatments can be considered perfect, mostly due to the presence of harmful side effects. Additionally, there is evidence to suggest that extended usage of these medications may result in a reduction of their effectiveness. One primary drawback associated with existing pharmaceutical treatments is the requirement for lifelong administration, which is accompanied by the occurrence of adverse effects. The utilisation of medicinal plants and their bioactive elements has been recognised as a viable approach for managing diabetes mellitus (DM) in various regions, particularly in nations where the availability of conventional anti-DM medications is limited[7]. There are several experimental paradigms that can be utilised for the assessment of plant-derived antidiabetic efficacy. The purpose of this review is to gain a more comprehensive understanding of diabetes mellitus, including its clinical manifestations, epidemiological statistics, complications, and the current therapy options available for managing the condition[8].

The management of diabetes mellitus is dictated by its etiopathology and is typically categorised as type 1 and type 2 diabetes mellitus. Individuals who possess a genetic predisposition or are undergoing concurrent pharmacological therapy, such as corticosteroids, are more likely to experience hyperglycemia[9]. The American Diabetes Association (ADA) has recently approved two methods for screening diabetes mellitus: a 2-hour oral glucose tolerance test and HbA1c testing. Observational studies have provided evidence of significant correlations between chronic hyperglycemia and poor clinical outcomes, as well as acute hyperglycemia in intensive care settings[10].

Nevertheless, the matter of maintaining strict glycemic control in this particular context is a subject of debate due to the heightened occurrence of hypoglycemia and the potential rise in morbidity and fatality rates. To ensure optimal glucose control in a patient with critical illness, it is recommended to maintain a glucose range of 140-180 mg/dL (7.8-10.0 mmol/L) with the administration of continuous intravenous insulin infusion[11].

II. TYPES OF DIABETES MELLITUS

- ***Type 1 Diabetes mellitus***

People who have type 1 diabetes mellitus (T1DM), a disease that accounts for 5-10% of all cases of diabetes, have an immune system that attacks and destroys the beta cells that are located in the islets of the pancreas[12]. These beta cells are responsible for the production of insulin. These beta cells are responsible for producing the hormone insulin. Because of this, there is a severe shortage of insulin all across the world. Both genetic predisposition and environmental factors, such as virus infection, toxins, and particular dietary components, have been implicated in the development of autoimmunity[13]. Diabetes type 1 can develop at any time in a person's life, but it is most prevalent in younger individuals.

- ***Type 2 Diabetes Mellitus***

About 90% of all cases of diabetes are attributable to type 2 diabetes mellitus (T2DM). People with type 2 diabetes often develop a condition known as insulin resistance, which is characterised by a diminished response to insulin[14]. When the body's insulin is unable to keep blood sugar levels from fluctuating, it responds by making more insulin. However, this countermeasure is eventually rendered ineffective, leaving the body susceptible to the development of type 2 diabetes[15]. Diabetes type 2 is more likely to occur in those who have reached the age of 45 or are older. In spite of this, it is becoming increasingly prevalent in younger people as a consequence of rising rates of obesity, inactivity, and diets high in energy content[16-18].

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- ***Gestationals Diabetes Mellitus***

High blood sugar during pregnancy is called gestational diabetes mellitus (GDM), however it is more frequently known as hyperglycemia in pregnancy. While it's possible to get gestational diabetes at any point in your pregnancy, your chances of getting it increase as your pregnancy progresses[19]. Only seven percent of pregnancies with gestational diabetes are reported to have no complications. Children of mothers with GDM are at increased risk for developing type 2 diabetes later in life.

GDM can lead to a number of different disorders, including hypertension, preeclampsia, and hydramnios; these conditions can also increase the risk that a surgical intervention will be required[20]. Macrosomia is characterized by an excessively large size or weight of the developing fetus. These newborns are at a higher risk for respiratory distress syndrome as well as becoming overweight as children and adolescents later in life[21]. The mother's advanced age, obesity, excessive weight increase during pregnancy, a previous history of birth abnormalities or stillbirth, and a history of diabetes in the family are all risk factors for gestational diabetes mellitus (GDM)[22][23].

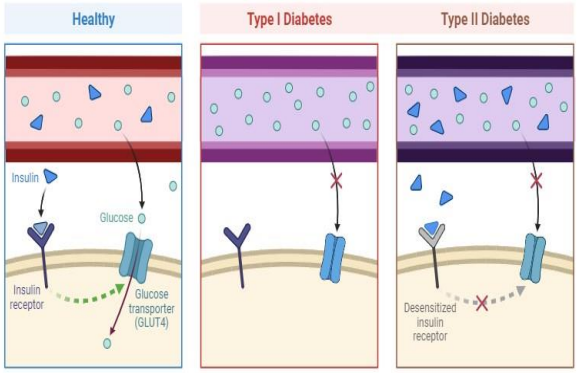

Fig 1: Healthy vs Type I Diabetes vs Type II Diabetes

III. PATHOPHYSIOLOGY OF DIABETES MELLITUS

Type 2 diabetes mellitus (DM) is distinguished by the presence of insulin insensitivity due to the development of insulin resistance, a decrease in insulin production, and eventual failure of the pancreatic beta cells.Consequently, there is a reduction in the transportation of glucose into the liver, muscle cells, and adipocytes. Hyperglycemia has been observed to be associated with an elevated rate of fat breakdown. The role of decreased alpha-cell function has lately been acknowledged in the pathophysiology of type 2 diabetes mellitus[24].

Due to this malfunction, the regulatory mechanisms that typically inhibit the elevation of glucagon and hepatic glucose levels during periods of fasting fail to be effectively reduced in the presence of a meal. Hyperglycemia occurs as a consequence of insufficient insulin levels and heightened insulin resistance. The incretins play a significant role as gastrointestinal mediators in the release of insulin, and specifically, in the inhibition of glucagon through GLP-1[25]. While individuals with type 2 diabetes mellitus (DM) experience reduced glucose-dependent insulinotropic polypeptide (GIP) activity, the insulinotropic effects of glucagon-like peptide-1 (GLP-1) remain intact. Consequently, GLP-1 may serve as a promising therapeutic intervention. Nevertheless, similar to GIP, GLP-1 undergoes fast inactivation by DPP-IV in vivo[26].

Two therapeutic strategies have been devised to address this issue: the development of GLP-1 analogues with extended half-lives, and the utilisation of DPP-IV inhibitors, which impede the degradation of both endogenous GLP-1 and GIP.Both categories of drugs have demonstrated potential, not only in normalising fasting and postprandial glucose levels, but also in enhancing beta-cell functionality and mass. Ongoing research is being conducted to investigate the involvement of mitochondrial dysfunction in the pathogenesis of insulin resistance and the aetiology of type 2 diabetes mellitus. Another crucial aspect to consider is the role of adipose tissue as an endocrine organ. This hypothesis suggests that adipose tissue secretes numerous adipocytokines, such as leptin, TNF-alpha, resistin, and adiponectin, which have been implicated in the development of insulin resistance and perhaps beta-cell dysfunction[27].

The majority of persons afflicted with type 2 diabetes mellitus exhibit obesity, characterised by central visceral adiposity. Hence, the adipose tissue assumes a pivotal role in the pathophysiology of type 2 diabetes mellitus. The prevailing explanation for this association is the portal/visceral hypothesis, which attributes a significant role to heightened amounts of non-esterified fatty acids. However, two recently developing hypotheses provide other explanations: the ectopic fat storage syndrome, characterised by the accumulation of triglycerides in muscle, liver, and pancreas cells. The aforementioned theories serve as the foundation for investigating the interaction between insulin resistance and beta-cell dysfunction in type 2 diabetes mellitus, as well as the relationship between our environment that promotes obesity and the likelihood of developing diabetes mellitus in the upcoming decade.

IV. EPIDERMIOLOGY OF DIABETES MELLITUS

Approximately 9% of the global population is diagnosed with type 2 diabetes, indicating that one person in every eleven individuals is affected by this condition on a global scale. The prevalence of type 1 diabetes (T1D) has a constant upward trend throughout

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an individual's lifespan, with the peak incidence occurring during early childhood (between the ages of 4 and 6) and adolescence (between the ages of 10 and 14)[28]. Approximately 45% of children manifest certain characteristics or behaviours prior to reaching the age of ten. Approximately 2.3% of individuals under the age of 20 are affected by this phenomenon. The observation that both genders have an equal likelihood of getting type 1 diabetes during childhood is surprising, considering that the prevalence of autoimmune diseases tends to be higher among females. Males of European descent aged 13 and above exhibit a potential threefold elevation in susceptibility to developing type 1 diabetes in comparison to females[29]. In recent years, there has been a noticeable increase in the prevalence of type 1 diabetes. In the regions of Europe, Australia, and the Middle East, an annual growth rate ranging from 2% to 5% is observed. The incidence of type 1 diabetes in the United States is experiencing a gradual rise of around 2% year across various age groups and ethnic backgrounds. Notably, the prevalence is more pronounced among Hispanic children and adolescents[30]. The underlying explanation of this trend is not readily apparent. Based on many measurements, including data from the United States Military Health System's data repository, it was observed that the prevalence of the condition remained constant between 2007 and 2012, with a rate of 1.5 cases per 1000 individuals. However, the incidence of the disease varied within the range of 20.7 to 21.3 cases per 1000 individuals[31].

Conversely, there exists a correlation between a surge in the incidence of type 2 diabetes among younger populations and a widespread occurrence of obesity among teenagers. This phenomenon is especially evident within younger demographic groups[32]. Diabetes type 2 has a prevalence of around 9 percent among the overall population in the United States, whereas among individuals aged 65 and beyond, the prevalence exceeds 25 percent. In 2015, the International Diabetes Federation reported that diabetes mellitus has a global prevalence of approximately one in eleven individuals aged 20 to 79 years[33]. The global population of individuals affected by diabetes presently stands at 415 million, with projections indicating a significant increase to 642 million by the year 2040[34]. Individuals who are transitioning from a state of poverty to a condition of relative wealth will encounter the most pronounced acceleration in the rate of their upward socioeconomic advancement[35]. The prevalence of type 2 diabetes is significantly higher among white Americans compared to Blacks, Native Americans, Pima Indians, and Hispanic Americans in the United States, with a two to six-fold difference[36]. Ethnicity is a significant determinant in the susceptibility to type 2 diabetes, nevertheless, it is important to acknowledge that environmental elements also exert a pivotal influence on the advancement of this condition[37]. In comparison to the United States, where the prevalence of type 2 diabetes mellitus (T2DM) among Pima Indians is reported to be 38%, the corresponding percentage in Mexico stands at a significantly lower 6.7%[38-40].

V. DIABETES MELLITUS GLOBAL BURDEN

The susceptibility to type 2 diabetes exhibits considerable variation across different regions, with Pacific Islanders, Asian Indians, and Native Americans demonstrating a notably elevated risk for the development of this condition. The prevalence of type 2 diabetes has exhibited a notable escalation on a global scale starting from the 1990s, with a substantial surge observed since the year 2000. Based on data provided by the International Diabetes Federation (IDF), it is seen that diabetes affects 8.8% of the adult population. Notably, the prevalence of diabetes is somewhat greater among males (9.6%) compared to women (9.0%). According to recent global figures, the prevalence of diabetes and impaired glucose tolerance (IGT), a precursor to diabetes, is estimated to be 463 million and 374 million individuals, respectively. The projected figures indicate that the global population affected by diabetes is expected to rise to around 700 million individuals, while the number of individuals with impaired glucose tolerance (IGT) is forecast to reach 548 million by the year 2045. This is a significant increase of 51% when compared to the figures recorded in 2019[41].

The International Diabetes Federation (IDF) has identified several locations with varying prevalence rates of diabetes. Notably, the Western Pacific region exhibits the highest number of individuals affected by diabetes, totaling approximately 163 million. Following closely is the South-East Asian region, with an estimated 88 million individuals affected. Europe ranks third in terms of diabetes prevalence, with approximately 59 million individuals affected. The Middle East and North Africa region follows closely behind, with an estimated 55 million individuals affected. Lastly, the North America and Caribbean region reports a prevalence of around 47.6 million individuals affected by diabetes. At present, the regions with the lowest numerical values are South and Central America, which have a total of 36.1 million individuals, and Africa, which has a population of 19.4 million. Hence, it is evident that the prevalence of the diabetes epidemic extends beyond the prosperous regions of Europe and North America[42].

Based on the IDF's data from 2019, it is evident that China, India, and the United States of America are the three countries with the largest diabetic populations. China reported a staggering 116.4 million individuals with diabetes, followed by India with 77.0 million, and the United States with 31.0 million. It is anticipated that the aforementioned pattern will persist in the years 2030 and 2045, wherein China is projected to have a burden of 140.5 and 147.2 million cases of diabetes, while India is forecast to have 101.0 and 134.2 million cases, hence

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maintaining their status as the countries with the highest prevalence of diabetes. This assertion is substantiated by the findings of the Global Burden of Disease Study, which documented that the expansion of populations and the process of population ageing in major nations, such as China and India, are the primary factors contributing to the overall rise in the prevalence of diabetes.

Based on prevalence figures provided by the International Diabetes Federation (IDF), it is observed that the burden of diabetes is increasing at a more rapid rate in low- and middle-income nations, with a total of 367.8 million individuals affected, compared to high-income countries where the number stands at 95.2 million. The Global Burden of Disease research, encompassing 195 countries and territories, furnished a comprehensive analysis of the quantitative aspects, including figures, rates, and upward trajectories, pertaining to the burden of diabetes from 1990 to 2025. This study also found that regions with low- and middle-income experienced a greater prevalence of diabetes, whereas regions with high-income had a lower prevalence of diabetes. According to the findings of this study, there was a significant rise in the prevalence of diabetes between the years 1990 and 2017[43]. Specifically, the number of individuals diagnosed with incident diabetes grew from 11.3 million to 22.9 million, representing a substantial growth of 102.9%. Additionally, the number of individuals living with prevalent diabetes also had a notable increase, rising from 211.2 million to 476.0 million, indicating a rise of 129.7% over the same time period. In addition, it was shown that the primary risk factors contributing to the burden of diabetes are metabolic, environmental, and behavioural factors that are subject to modification.

VI. CONCLUSION

Diabetes mellitus (DM) is a metabolic disease characterised by a variety of forms, each originating from independent pathophysiological mechanisms. However, these forms commonly show as a disorder with overlapping and challenging-to-distinguish characteristics. The therapy and management approaches for each kind of diabetes exhibit distinct characteristics, yet also demonstrate significant similarities, mirroring the nature of the condition itself. The aforementioned highlights the significance of accurate and prompt diagnosis of each variant of diabetes, as well as the crucial role played by comprehending their pathophysiology. It is crucial to protect persons with diabetes from the potential negative consequences of inappropriate, ineffective, or preventable pharmaceutical therapies, as these can often hinder the desired prognosis and prolong periods of hyperglycemia. Long-term hyperglycemia has frequently been linked to an elevated risk of both microvascular and macrovascular diabetic complications. These consequences have a significant impact on individuals' quality of life and are major contributors to the morbidity and mortality associated with diabetes. The accurate and timely molecular diagnosis of diabetes, including the types caused by genetic mutations or associated genetic anomalies, can contribute to the analysis of disease risk and facilitate the prediction and early identification of individuals who are at a heightened risk of developing the disorder, particularly among their family members. Diabetes has emerged as a prominent and pressing public health concern on a global scale. Particularly in low- and middle-income countries such as India, the prevalence of diabetes has experienced a substantial increase in recent decades, with projections indicating a continued upward trajectory in the years to come. The potential impact of this intervention on the morbidity and mortality rates related to diabetes, and subsequently on the healthcare spending in India, is significant. In order to address the widespread prevalence of diabetes and its consequential complications, it is imperative to implement a comprehensive approach that encompasses several key components. These include timely identification of diabetes through early diagnostic measures, thorough screening for associated complications, and the provision of optimal therapeutic interventions across all levels of healthcare for individuals already diagnosed with diabetes. Additionally, primary prevention strategies targeting individuals with prediabetes are crucial in mitigating the onset of diabetes.

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