

Diabetes Mellitus: A Review

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Abstract- *Diabetes mellitus is a chronic non-communicable disease which is a crucial factor for mortality and curtailed life expectancy. Diabetes is the outcome of a complicated interaction of environmental, behavioural, and hereditary factor. Diabetes Mellitus increases at an increasing rate if appropriate measures are not taken. The prevalence of diabetes not only poses significant risks to public health, but also has a severe adverse impact on social and economic progress worldwide. As a result, multisectoral initiatives and efficient interventions are crucial for preventing and treating diabetes. The global burden of diabetes must be reduced by early prediction, appropriate knowledge, and healthcare policy. This article provides a systematic review of definition, types, global burden and economic impact of diabetes.*

I. INTRODUCTION

Diabetes mellitus is derived from Greek word diabetes, which means siphon or pass through and the Latin term mellitus, which means sweet[1].The sweetness of the urine in this disease was discovered by the ancient Greek, Indian, and Egyptian civilizations, leading to the spread of the term diabetes mellitus[1].One of the most prevalent non-communicable disease around the world is "diabetes mellitus" affecting more than 100 million people globally (6% of the population)[2,3].Due to a lack of information and understanding about this chronic disorder, India also has a large population of patients with diabetes mellitus[4].Thus, India is regarded as the diabetes capital of the globe[5]. Diabetes is a chronic condition that results from either inadequate insulin production by the pancreas (type I diabetes) or ineffective insulin utilisation by the body (type 2 diabetes)[6].Diabetes refers to a category of metabolic conditions that are recognised and distinguished by the presence of hyperglycemia in the absence of medication.Diabetes might manifest with clinical features such as thirst, polyuria, blurred vision, and weight loss[7]. In addition to problems in the metabolism of carbohydrates, fats, and proteins, the diverse aetiopathology also includes defects in insulin secretion, insulin action, or both.Among other implications, the long-term clinical effects of diabetes include retinopathy, nephropathy, and neuropathy[2].According to the report, 90% of diabetic individuals also have other chronic diseases. Particularly, those with diabetes have increased rates

of hypertension[6].Insulin and oral hypoglycemic medications are two of the pharmacotherapies for diabetes mellitus that are currently accessible[3]. These medications either lower plasma glucose concentrations by boosting glucose absorption and gluconeogenesis or by increasing insulin production from the pancreas[3].However, the existing medications do not maintain normal glucose homeostasis for an extended period of time, and they have side effects such hypoglycemia, kidney disease, GIT issues, hepatotoxicity, heart risk issues, and insulinoma that require lifelong use[3].Compared to the northern and eastern regions, the disease seems to be more abundant in the south of the nation[5]. Type 1 DM, also known as insulin-dependent diabetes mellitus (IDDM), is perhaps the most common type of diabetes and requires daily insulin injections or the use of an insulin pump because it is an insulin-dependent condition. This condition is also known as "juvenile diabetes." Insulin resistance, which occurs when cells improperly utilise insulin with or without an absolute insulin deficit, is the cause of type 2 diabetes mellitus, also known as non-insulin-dependent diabetes mellitus (NIDDM). The term "adult-onset diabetes" was originally used to describe this type. Gestational diabetes, the third major kind, develops when pregnant women with no prior history of diabetes have high blood glucose levels[3]. Current WHO recommendations for the diagnostic criteria for diabetes and intermediate hyperglycemia:

TABLE

Diabetes (type 1 and 2)	Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dl) or 2 hours plasma glucose ^a ≥ 11.1 mmol/L (200 mg/dl) or HbA1c $\geq 6.5\%$
Impaired glucose tolerance (IGT)	Fasting plasma glucose < 7.0 mmol/L (126 mg/dl) and 2 hours plasma glucose ^a ≥ 7.8 and < 11.1 mmol/L (140 mg/dl and 200 mg/dl)
Impaired fasting glucose (IFG)	Fasting plasma glucose 6.1 to 6.9 mmol/L (110 mg/dl to 125 mg/dl) and (if measured) 2 hours plasma glucose ^a < 7.8 mmol/L (140 mg/dl)

Gestational diabetes (GDM)	One or more of the following: Fasting plasma glucose 5.1–6.9 mmol/L (92–125 mg/dl) 1-h plasma glucose ^b ≥ 10.0 mmol/L (180 mg/dl) 2-h plasma glucose ^a 8.5–11.0 mmol/L (153–199 mg/dl)
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CLASSIFICATION:

Although categorization of diabetes is crucial and influences treatment approaches, it is a challenging task because many individuals, particularly younger adults, do not easily fit into a single class[8]. Diabetes Mellitus is classified into 3 types which includes type 1 diabetes, type 2 diabetes, gestational diabetes.

TYPE 1 DIABETES MELLITUS:(T1DM)

T1DM is most prevalent in young people, accounting for more than 85% of diabetic cases in people under 20 years of age worldwide[9]. In children and adolescents, type 1 diabetes makes up 80–90% of cases of diabetes[8]. The chief cause of type 1 diabetes is an autoimmune response on pancreatic β cells that is triggered by both a humoral and inflammatory T-cell response[8]. In order to treat type 1 diabetes, which is characterised by loss of insulin secretion due to idiopathic assault or autoimmune destruction of insulin-secreting beta cells of the islets of Langerhans in the pancreas, insulin replacement treatment is the major method used and so it is called as insulin dependent diabetes mellitus[10]. According to a Swedish study, individuals with T1DM who were diagnosed before the age of 10 had a three-fold higher mortality rate than the controls, whereas patients diagnosed between the ages of 26 and 30 had a less than two-fold higher mortality rate than the controls[9]. T1DM cuts down life expectancy in high-income countries by roughly 13 years[7]. In comparison to adults, children experience more severe symptoms[11]. In children and adolescents, type 1 diabetes can cause symptoms such polydipsia, polyuria, enuresis, lack of energy, intense fatigue, polyphagia, abrupt weight loss, poor wound healing, recurring infections, and blurred vision, as well as severe dehydration and diabetic ketoacidosis[12]. In nations with very little access to insulin, the prognosis is far worse[7]. The distinction between T1DM and T2DM in adults can be challenging, and estimates of prevalence and incidence may be impacted if T1DM is mistakenly labelled as T2DM or vice versa[7]. Some people have a quick rate of β -cell degeneration, whereas others have a sluggish rate. Children frequently experience the fast progressing version of T1DM, although adults can get it. Ketoacidosis may be the first sign of the condition in some people, particularly children and adolescents. Some people

may experience mild hyperglycemia that, in the event of an illness or another stressful situation, can abruptly worsen into severe hyperglycemia and/or ketoacidosis. The clinical traits of these people included a lower body mass index, the usage of insulin within a year of diagnosis, and a greater risk of diabetic ketoacidosis[7].

TYPE 2 DIABETES MELLITUS:(T2DM)

The most prevalent kind of diabetes worldwide is type 2[10]. In low- and middle-income nations, the prevalence of T2DM is highest, accounting for 90% to 95% of all diabetic cases[7]. Although numerous cases of it have lately been found in obese children, it specifically targets adults over the age of thirty[10]. Children and adolescents are now extremely affected by T2DM, which was initially diagnosed in adults[9]. This kind of diabetes directly impacts between 90% and 95% of individuals, the majority of whom are adults[8]. Historically, type 2 diabetes was sometimes referred to as non-insulin-dependent diabetes mellitus (NIDDM) or late onset diabetes, however these terms are no longer used owing to the risk of misconception if patients were grouped according to pathogenesis rather than therapy[10]. Since insulin secretion continues and insulin depletion is minimal, the significant proportion of type 2 diabetes patients do not require insulin. One of the most significant differences from type 1 diabetes is the reliance on insulin[8]. The revolutionary Search for Diabetes in Youth study revealed that T2DM with early onset is aggressive in character. Consequently, a higher lifetime exposure to hyperglycemia is probably linked to a higher risk of complications. According to the reliable data, it is desirable to avoid or postpone the development of T2DM since it is likely that younger age of T2DM onset is related with higher all-cause mortality[9]. The fundamental cause of the upsurge in type 2 diabetes cases among young people is the switch in children's lifestyles toward a more sedentary manner of living and less nutritious diet. Insulin resistance, the predominant cause of type 2 diabetes, is most commonly caused by obesity[13]. In nations where routine checkups without symptoms are not part of the culture, type 2 diabetes is frequently diagnosed years after the onset of its mild symptoms. Since hyperglycemia is not treated during this undetected time, this delay in diagnosis could lead to even more type 2 diabetes patients acquiring long-term issues. Type 2 diabetes had been misinterpreted for type 1 diabetes since it can occur in children and adolescents who are not obese, as well as it can occasionally cause severe dehydration and ketoacidosis in some paediatric patients with type 2 diabetes[8]. It is a widespread and serious global health issue that has arisen in connection with rapid cultural, economic, and social change, ageing populations, rapid urbanisation that hasn't been planned for, dietary changes—such as an increase

in the consumption of highly processed foods and sugar-sweetened beverages—obesity, decreased physical activity, unhealthy lifestyle and behavioural patterns, foetal malnutrition, and a rise in the exposure of foetuses to high blood sugar during pregnancy. Individuals from low- and middle-income nations, like India, as well as those of Indian origin residing in high-income nations, have also been found to exhibit beta dysfunction[7].

GESTATIONAL DIABETES:

When pregnant women experience their first signs of glucose intolerance, gestational diabetes mellitus (GDM) emerges. Along with an increase in the frequency of obesity and overweight in women of reproductive age, the prevalence of gestational diabetes is rising. There have been no studies that have examined the link between gestational diabetes and all-cause mortality, despite the fact that it is a significant risk factor for developing T2DM in the future. The risk of acquiring diabetes later in life is higher for newborns whose moms have gestational diabetes. The risk of macrosomia (birth weight 4.5 kg), large-for-gestational-age births, preeclampsia, premature birth, and caesarean delivery due to large infants is increased throughout pregnancy due to hyperglycemia. Obesity, a personal or family history of gestational diabetes, maternal age, polycystic ovarian syndrome, a sedentary lifestyle, and exposure to hazardous substances are risk factors for gestational diabetes.[8-13]

TABLE - 1:

AGE GROUP	TYPE OF DIABETES
Below 6 months	<ol style="list-style-type: none"> 1. Monogenic neonatal diabetes (transient or permanent) 2. Type 1 diabetes (extremely rare)
6 months - less than 10 years	<ol style="list-style-type: none"> 1. Type 1 diabetes 2. Type 2 diabetes (rare before puberty) 3. Monogenic neonatal diabetes (transient or permanent)
10 years - less than 25 years	<ol style="list-style-type: none"> 1. Type 1 diabetes 2. Type 2 diabetes 3. Monogenic diabetes
25 years - 50 years	<ol style="list-style-type: none"> 1. Type 1 diabetes 2. Type 2 diabetes
Greater than 50 years	<ol style="list-style-type: none"> 1. Type 1 diabetes 2. Type 2 diabetes

GLOBAL BURDEN OF DIABETES:

The biggest threat to global health is diabetes. Over the past four decades, prevalence of diabetes has significantly expanded on a global scale[14]. Every country and location in the world has a population with diabetes. Diabetes has a massive and expanding economic cost worldwide. In industrialised nations, the number of adults with diabetes would rise by 20 percent, whereas in underdeveloped nations, it would rise by 69 percent[15]. This rising diabetes trend was uneven across nations and regions[16]. The estimates portrayed a picture of the future burden of diabetes that was ever more worrisome as it was revealed that each estimate of the number of individuals with diabetes had been underestimated[17]. Premature mortality, morbidity, psychological discomfort and sadness, as well as financial loss are reflected in the Global Burden. Rapid urbanisation, population ageing, socioeconomic change, and dietary and nutritional factors are the key causes of the rise in this disease burden[6]. Middle-aged working persons would account for a large portion of the increase in the number of people with diabetes. In terms of diabetes, men outnumber women by a small margin (215 million men vs. 200 million women). Urban areas currently have 270 million more persons with diabetes than rural areas do (145 million)[15]. Diabetes spreads more quickly in low- and middle-income countries (LMICs) than in high-income countries[6]. Not every diabetic has received a diagnosis. One in two persons throughout the world are thought to have undiagnosed diabetes. The percentage of diabetics who are undiagnosed might reach up to 67% in areas with limited access to healthcare, such as sub-Saharan Africa. A little over one-third of persons with diabetes go undiagnosed, even in high-income areas like North America. 81 percent of undiagnosed diabetics worldwide reside in low- and middle-income nations[18,15]. Diabetes mellitus incident cases have increased by 102.9% globally from 11,303,084 cases in 1990 to 22,935,630 cases in 2017[16]. Diabetes alone is responsible for almost 1 million fatalities annually, ranking it as the ninth most common cause of death[19]. People under the age of 60 account for over half of deaths from diabetes, which is one of the top ten killers [6]. Diabetes expenses account for a portion of an individual's income. The value of lost productivity (indirect costs) resulting from diabetes and its consequences was added to excess medical costs (direct costs) to determine the entire economic burden of diabetes[14].

Mathematically,

Total economic burden of diabetes = excess medical expenses + loss of productivity due to diabetes

Projections of diabetes in top 10 countries in 2030 and 2045 is represented in the table given below:

Top 10 countries or territories for number of people with diabetes (20–79 years) in 2019, 2030 and 2045

2019 Rank	Country or territory	Number of people with diabetes, Million	2030 Rank	Country or territory	Number of people with diabetes, Million	2045 Rank	Country or territory	Number of people with diabetes, Million
1	China	116.4 (108.6–145.7)	1	China	140.5 (130.3–172.3)	1	China	147.2 (134.7–176.2)
2	India	77.0 (62.4–96.4)	2	India	101.0 (81.6–125.6)	2	India	134.2 (108.5–165.7)
3	United States of America	31.0 (26.7–35.8)	3	United States of America	34.4 (29.7–39.8)	3	Pakistan	37.1 (15.8–58.5)
4	Pakistan	19.4 (7.9–30.4)	4	America Pakistan	26.2 (10.9–41.4)	4	United States of America	36.0 (31.0–41.6)
5	Brazil	16.8 (15.0–18.7)	5	Brazil	21.5 (19.3–24.0)	5	America Brazil	26.0 (23.2–28.7)
6	Mexico	12.8 (7.2–15.4)	6	Mexico	17.2 (9.7–20.6)	6	Mexico	22.3 (12.7–26.8)
7	Indonesia	10.7 (9.2–11.5)	7	Indonesia	13.7 (11.9–14.9)	7	Egypt	16.9 (9.0–19.4)
8	Germany	9.5 (7.8–10.6)	8	Egypt	11.9 (6.4–13.5)	8	Indonesia	16.6 (14.6–18.2)
9	Egypt	8.9 (4.8–10.1)	9	Bangladesh	11.4 (9.4–14.4)	9	Bangladesh	15.0 (12.4–18.9)
10	Bangladesh	8.4 (7.0–10.7)	10	Germany	10.1 (8.4–11.3)	10	Turkey	10.4 (7.4–13.2)

! Confidence intervals are presented in brackets.

ECONOMIC IMPACT OF DIABETES:

The financial burden of diabetes is tremendous[20]. Healthcare costs are increasing along with a country's economic prosperity[15]. Diabetes-related expenses can be divided into three categories: direct costs, indirect costs, and intangible costs[7]. In direct cost, all expenses incurred in providing care and/or assistance to people with diabetes. Costs for both medical and non-medical expenses are included[5].50% of the direct costs are made up of medication costs[7].A country's per capita gross domestic output is significantly correlated with the direct costs of diabetes[21]. According to the WHO Global Burden of Diabetes Report, diabetes directly costs the globe more than US\$ 827 billion each and every year[6]. In indirect cost, All expenses related to productivity losses brought on by diabetes-related morbidity and mortality. In intangible cost, the expenses correlated with all the negative effects of the ailment that impact patients' quality of life[5]. Diabetes complications potentially threaten a person's health and life if they are not handled appropriately[6].The global rise of type 2 diabetes has significant effects on the cost of healthcare. The demand and per capita expenses for the treatment of diabetes and its impact will significantly rise as low- and middle-income countries experience economic growth. Most nations allocate 5% to

20% of their overall healthcare budgets on treating diabetes and its complications[15].Among the studies, 63% examined the overall expenditures of diabetes, 21% only examined its consequences, such as diabetic foot wound (DFW) and chronic renal disease, and 16% examined the cost of a particular medicine used to treat diabetes. Foot issues were the most expensive of the several difficulties examined; patients with foot complications incurred four times much more than patients without complications. Spending was three times higher in patients with renal failure, cardiovascular difficulties, and retinal issues than in those without complications[5].Antihyperglycemic therapy costs a significant absolute sum but only makes up a modest fraction of overall healthcare spending in developed nations with high mean annual health care expenditures. The treatment of complications and comorbidities accounts for the majority of healthcare costs associated with diabetes. In contrast, the majority of healthcare spending in developing nations with low mean annual health care expenditures goes toward antihyperglycemic medication[22].Care for diabetes is more expensive than the average healthcare budget per individual by at least 3.2 times, and by 9.4 times if complications are detected[23]. India's government spends the least on public health compared to other countries. As a result, 70% of all health expenses are made up of out-of-pocket (OOP) expenses. Because of this, more than 70% of diseases in India's rural and urban areas are mostly funded and provided by the private sector[20]. The chief expenses for these costs are given in the table 3.The majority of the evaluated studies included in the analysis support the claim that the major factor for these disproportionately high drug costs is doctors' widespread preference for brand-name drugs over generic alternatives[24].

TABLE 3:

S. NO	TYPE OF COST	EXPENDITURE
1.	Direct cost	Drug cost, hospital related cost, consultation cost, laboratory cost, transportation cost.
2.	Indirect cost	Productivity loss, premature mortality, absenteeism.
3.	Intangible cost	Isolation, pain, anxiety, affects quality of life.

II. CONCLUSION

To raise awareness, prepare for future requirements, and inform solutions, we must comprehend the global burden of diabetes. Since diabetes is a lifestyle disease, changing one's eating habits, level of physical activity, beliefs, and behaviour can lessen the financial strain. The need for multi sectoral methods to combat diabetes is critical given that there are 500 million individuals globally who have the disease. It is estimated that 578 million people will have diabetes by 2030, and that figure will rise by 51% (700 million) by 2045 if prompt and effective measures are not taken. Considering the high prevalence of diabetes-related disabilities and comorbidities, it is crucial to create practical preventative methods. Governments, organisations, communities, and people must put forth effort and perseverance. One should not undervalue the intricacy of diabetes prevention programmes and policies. It is essential to allocate equivalent financial resources in healthcare budgets for diabetes prevention and treatment. Perhaps more cost-effective strategies include enhancing primary care and redesigning communities to promote active living and a healthy diet. At the national level, active measures must be taken to combat this epidemic, including funding for public health, public policy, and financial incentives for local communities to launch diabetes prevention initiatives. According to studies, any measures taken to minimize hospitalisation expenses will significantly lessen the financial pressure on households and society while also improving the quality of life for patients. Better health care coverage is necessary since patients and their families bear a heavy financial burden.

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