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A Review of the Diabetic Status in India

Praveen Kumar Gupta[1*], Sonnahallipura Munivenkatappa Byregowda[2], Archana. Munivenkatarayappa[3], Raju Hanumegowda[1], Chandrananthi Chithananthan[4], Shravani S Daptardar[4], Joanna Nicole D'Souza[4], Vanam Rashmi[4], Faheena Anjum N Jahangir[4], Sarah Philip[4], Yasmin Khatoon[5]

[1]Assistant Professor, Department of Biotechnology, R.V College of Engineering, Bangalore-560059, India.
[2]Director, Institute of Animal Health and Veterinary Biologicals, Bangalore, India.
[3]Assistant Professor (opg), Small animal House, Institute of Animal Health and Veterinary Biologicals, Bangalore, India.
[4]Research Scholar, Department of Biotechnology, R.V College of Engineering, Bangalore-560059, India.
[5]Assistant Professor, Department of Pharmacy, Rameshwaram Institute of Technology and Management, Lucknow, Uttar Pradesh, 227202, India.

Abstract

Objective: Diabetes mellitus (DM) also known as diabetes, is a chronic metabolic disorder that is rapidly becoming a worldwide concern with severe economic, social, and health consequences. Diabetes is a collection of metabolic illnesses defined by hyperglycemia that results due to abnormalities in the secretion of insulin, its action, or a combination of the two. According to the International Diabetes Federation (IDF), there were around 387 million diabetics worldwide in 2014, with that number anticipated to climb to 592 million by 2035. Additionally, the fact that over half of the population has diabetes that goes undiagnosed adds to the difficulty of diagnosis. Diabetes is already on the increase in India as a result of a combination of genetic predisposition and lifestyle changes brought about by globalization and urbanization. Even though diabetes affects a large section of India's population, diabetes awareness campaigns are few and far between, although it is one of the most severe issues to be addressed. Regular exercise, stress management, yoga, and regular exercise, as well as mindful nutrition, are all important aspects of diabetes control. This research gives an overview of the current status of diabetes in India, as well as the influence of nutrition, geographic distribution, and air pollution on the spread of the disease. It also addresses some of the diabetic therapies.

Keywords: Diabetes mellitus, Geographical distribution, Diet, Air pollution, Prevention, Treatment

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Corresponding Author:
Praveen Kumar Gupta, Assistant Professor, Department of Biotechnology, R.V College of Engineering, Bangalore-560059, India.
Tel: (91) 974 262 0113
Email: praveenkgupta@rvce.edu.in
Orcid ID: 0000-0003-0972-1384

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder that has been around for almost 3000 years (1). Cases of excessive sugar were discovered in the blood and urine of various patients in the United Kingdom in 1776 (2). Diabetes is a long-term metabolic condition characterized by hyperglycemia. Hyperglycemia is caused by either a lack of insulin production or defective insulin activity (3). Due to the different complications, it is the fourth leading cause of death globally. If not treated, diabetes can cause damage to many organs, including the kidneys, eyes, cardiovascular system, and nerves.

DM can be divided into three major subdivisions based on the clinical features and etiology: Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), and Gestational Diabetes Mellitus (GDM). T1DM occurs when there is a cellular-mediated autoimmune response that leads to the destruction of the cells in the pancreas, resulting in inadequate amounts of insulin produced. Patients diagnosed with T2DM have insulin resistance and relative insulin insufficiency. GDM occurs during pregnancy when patients experience some degree of glucose tolerance. Studies have shown that populations of Indian origin are more susceptible to diabetes than practically any other population. As the living conditions in India are improving, we are progressively adopting western dietary habits, along with a sedentary lifestyle and an increased susceptibility to psychological stress, which are unsuitable for our environment (4).

As a result, over the past few decades, India has seen unprecedented growth in the prevalence of diabetes. High levels of hemoglobin A1c (HbA1c) were discovered to be one of the primary risk factors in T2DM for macrovascular and microvascular problems. Diet management can help patients with their elevated HbA1c levels, which can prevent them from acquiring diabetes comorbidities (5). A diabetic patient is also at risk for renal and heart disease.

Their life expectancy is only about 8 years following the commencement of the disease. Constant migration and economic boom lead to changes in lifestyle and contribute to the growing number of diabetic patients in the country, who are frequently diagnosed during adolescence, increasing morbidity and mortality and lowering patients' standard of living (6).

Monogenic diabetes is oftentimes misdiagnosed as T1DM or T2DM with early onset. It generally happens when a single gene or chromosomal anomaly has one or more mutations. Maturity-onset diabetes of the young (MODY) and neonatal diabetes are both caused by a decrease in beta cells or mass. MODY accounts for 1-3% of diabetes diagnosed in people under the age of 30 (0.4% of all diabetes), with a prevalence of 1:90,000–1:25,000 (7). Specific medications and management techniques exist for the most common monogenic diabetes, which can improve glycemic control and reduce complications, resulting in better health outcomes for those affected. Monogenic diabetes allows adopting a precision medicine approach to enhance diabetes drug selection and management, hence improving glycemic outcomes for afflicted people while also reducing the burden and expense of care. Continued study into diabetes that is caused by single-gene changes can also help us understand the causes of polygenic diabetes and also help us categorize the heterogeneous representations of T2DM for guiding first-line medication selection and introducing precision medicine in diabetes (8).

Current status of diabetes

In India, where more than 62 million people have been diagnosed with diabetes, the disease is on the verge of becoming an epidemic. In the year 2000, India topped the world with the greatest number of diabetics (20.8 million), followed by China (20.8 million), and the

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United States (19.8 million). One out of every four diabetic patients is expected to be Indian.

According to Wild et al., the number of people living with diabetes is expected to double globally from 171 million in 2000 to 366 million in 2030, with India seeing the largest growth. Despite having lower rates of overweight and obesity, India has a greater prevalence of diabetes than Western countries. Due to low levels of high-density lipoproteins and dyslipidemia, Indians are genetically prone to coronary artery disease. As a result, Indians are more likely than Caucasians to have diabetic problems at a young age (20-40 years). Regardless of the patient's age, it is critical to screen and monitor the incidence of diabetes in India. (Kaveeshwar & Cornwall, 2014). Many Saudi Arabians are getting obese as a result of their intake of fast food and sugary drinks, which has resulted in alarming diabetes statistics. (Sami et al., 2017). According to studies, diabetes is more common in migratory Indians than in local host groups. Plasmodium falciparum cases in patients with DM have increased in developing countries, such as Sub-Saharan African countries. The occurrence of two such diseases has resulted in a rise in morbidity and mortality (9). According to the IDF in 2019, the top three countries with the highest number of individuals with diabetes are China (116.4 million), India (77.0 million), and the United States of America (31.0 million). This trend is expected to continue in 2030 and 2045, with China (140.5 and 147.2 million) and India (101.0 and 134.2 million) continuing to have the highest burden of diabetes (10).

Causes of diabetes

Weight and body type: Being overweight and obese are the leading causes of T2DM and GDM, respectively. A large buildup of fat in the abdominal regions causes insulin resistance and metabolic syndrome. According to recent studies, a rise in childhood obesity is to blame for the increased occurrence of T1DM (11).

Sex: According to the National Institute of Health (NIH), males account for 53% of adult diabetes cases in the United States. One possibility is low testosterone levels (male hypogonadism), which researchers have linked to insulin insensitivity (12).

Regular exercise: Lack of physical exercise can lead to obesity, which can increase the likelihood of diabetes (13).

Diseases: T2DM is linked to medical disorders such as hyperlipidemia, high blood pressure, asthma, polycystic ovarian syndrome, and sleep apnea. Secondary diabetes can be induced by hemochromatosis, pancreatitis, endocrine illnesses such as Cushing's disease, hyperthyroidism, and acromegaly, and hereditary abnormalities such as diabetic foot, muscular dystrophy, and urinary tract infection (14).

Stress Hormones: In T2DM, stress hormones such as cortisol alter glucose levels, and stress hormones in pregnant women can induce T1DM in their children (5). Some teenagers may be more prone to disease as a result of the release of sex and growth hormones during puberty. Secondary diabetes is linked to hormonal therapies such as growth hormone, anabolic steroids, injectable contraceptives, estrogens, and androgen deprivation therapy for prostate cancer (15).

Alcohol: Besides these, diabetes can be caused by cigarette smoking and excessive alcohol intake (16). Alcohol inhibits glycogenolysis and gluconeogenesis in diabetic and non-diabetic patients. In type 2 diabetic patients, alcohol consumption, whether with or without meals, can result in high or low sugar levels, prompting an insulin response. Preconception alcohol exposure causes mutations in the genome that can result in severe abnormalities in the metabolic function of the children, hence increasing vulnerability to T2DM and disrupting glucose homeostasis in the offspring (17).

Smoking: Tobacco smoke is linked with a major risk of insulin resistance and diabetes. The compound nicotine is examined as a link between cigarette smoking and the progression

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of diabetes. However, smoking has not been regarded as a risk factor for diabetes. Furthermore, it is crucial to determine if smoking alters the hereditary risk of developing diabetes (18).

Medical Treatments: Diabetes can be exacerbated by drugs that are routinely used in medical practice. Although drug-induced hyperglycemia is usually mild and asymptomatic, it can progress to severe hyperglycemia and, as a result, diabetes acid ketosis (19). Concerning glucose metabolism, the medications can either activate insulin-resistant pathways or suppress insulin production.

Statins: Patients who consume statins have a higher risk of getting diabetes. When comparing patients on mild and intensive statin therapy, it was discovered that those on moderate doses had a greater chance of acquiring diabetes. More research is needed to be carried out on statins' method of action (20).

Niacin: For many years, niacin has been recognized to develop insulin resistance. The mechanism, however, is uncertain. The rebound elevation of fatty acids with treatment or the buildup of diacylglycerol is two possible explanations (21).

Pentamidine is an antiprotozoal drug that can produce both hyperglycemia and hypoglycemia. It is assumed to have a cytolytic influence on beta cells of the pancreas, resulting in the release of insulin and hypoglycemia, followed by beta cell destruction and insulin shortage, leading to diabetes (22).

In very rare cases, alpha interferon can lead to the development of T1DM (23). Various research studies have proved that second-generation antipsychotic drugs can contribute to T2DM. The various ways are: (1) induce obesity, (2) suppress insulin signaling, and (3) cause direct destruction of the -cells (24).

Androgen deprivation therapy: This therapy has been associated with an increased risk of diabetes in multiple studies. Insulin resistance is induced, possibly as a result of increases in pro-inflammatory adipokines such as interleukin-6, tumour necrosis factor-alpha, and resistin and/or visceral fat mass (25).

Mechanistic Target of Rapamycin Inhibitors (mTOR inhibitors): Diabetes has been linked to everolimus, sirolimus, and mTOR inhibitors. Insulin resistance and a decrease in insulin production are the adverse effects of these inhibitors on the metabolism of glucose (26).

Asparaginase: Hyperglycemia can be caused by asparaginase therapy. Asparaginase treatment can cause diabetic ketoacidosis, but this is not a common event. Hyperglycemia can be caused by enhanced insulin resistance, decreased insulin production, or increased glucagon secretion. Asparaginase can also cause pancreatitis, which can result in hyperglycemia (23).

Chemicals: Insulin resistance and T2DM are linked to chemicals like pesticides, Polychlorinated biphenyls like dioxin, and defoliant agent orange. Commercial plastics and plastic components such as bisphenol and phthalates have been related to insulin resistance in some circumstances. Pyramidal, a rat poison, has been linked to T1DM (27).

Environmental factors: Free radicals play a significant role in inducing T1DM and other types. As a result of the build-up of radicals, cells, particularly those involved in insulin synthesis, are destroyed. In cold environments, T1DM occurs more commonly and develops more commonly in the winters than in the summers (28).

Air Pollution**:** A higher incidence of DM and IR has been found in prospective cohort studies of patients exposed to 2, 3, 7, or 8-tetrachlorodibenzo-p-dioxin or other organic pollutants in occupational and other settings. Over six published epidemiologic studies show a link between PM-or traffic-related air pollution and DM to some extent. Diabetic individuals are more vulnerable to air pollution-related cardiovascular mortality and morbidity. Endothelial function is altered by air pollution in both animals and humans, and this alteration is commonly accompanied by

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alterations in IR, resulting in decreased peripheral glucose absorption (37).

Viruses: T1DM can be caused by certain viruses like coxsackievirus, rubella, and mumps. It is essential for diabetics and their families to have a better understanding of how viral, bacterial, and yeast-like fungal infections affect a child's or adolescent's risk of developing T1DM as well as the discovery of new risk factors, particularly those that are transmitted through droplets (29).

Diabetes in India based on geographical distribution

Diabetes has a wide range of causes, including hereditary factors as well as environmental influences such as obesity-related rising living standards, lifestyle changes, and persistent urban migration in India. The diabetes pattern is linked to the geographical distribution of diabetes in India. According to some estimates, diabetes affects 25% of the population in India and adjacent Indian subcontinent countries like Bangladesh, Nepal, Bhutan, and Sri Lanka. Kashmir Valley (Northern India), 11.7% in Kolkata (Eastern India), 11.6%t in New Delhi (Northern India), 13.5% in Chennai (South India), 9.3% in Mumbai (West India), 16.6% in Hyderabad (South India), and 12.4% in Bangalore (South India) (Kaveeshwar & Cornwall, 2014). The difference could be explained by the fact that South Indians are host populations, whereas North Indians are Asian communities migrating northward. Urban locations have access to reliable screening methods and anti-diabetic medications, but rural areas have food instability, illiteracy, inadequate sanitation, and a high frequency of communicable diseases, resulting in poor diabetes screening and prevention services. Diabetes prevalence was 1.6% in a house-to-house study conducted in Eluru, Andhra Pradesh (1.9% in males and 1.4% in females). (Rao, 2005).

COVID-19 and diabetes

According to current Italian statistics, diabetes was present in more than 67% of those who died from COVID-19. Individuals with diabetes have a higher risk of developing a severe or critical condition, as well as a higher mortality rate, according to clinical trials of COVID-19 patients diagnosed with diabetes. Diabetes history and hyperglycemia were also discovered to be independent predictors of COVID-19 death. The severity of COVID-19 infection in diabetes was thought to be disguised by a milder symptom of SARS-CoV-2 infection, with a lack of specific clinical signs, which could result in a life-threatening delay in receiving necessary treatment. Obesity, hypertension, coronary artery disease, and other diabetes-related chronic comorbidities may all contribute to the increased severity of COVID-19 in diabetics (30).

Role of diet in diabetes

Diabetes knowledge includes information on eating habits, weight monitoring, blood glucose levels, and the management of diabetes complications. Native medicinal experts prescribe neem tree leaves, bitter gourd juice, honey, and other natural diabetic therapies (31). Vegetable oils such as coconut oil are commonly utilized for cooking in Kerala, Malaysia, and Guyana, which is closely linked to a substantial rise in diabetes prevalence among the people selected from these places.

A few studies have established a substantial link between T2DM and high carbohydrate and fat diet. Recent studies have linked soft drink use to obesity and diabetes due to the use of massive volumes of high fructose corn syrup in soft drink production, which increases blood glucose levels, insulin resistance and BMI to harmful levels. Obesity is linked not just to the amount of food consumed but also to the constituents and quality of the diet. The consumption of red meat, sweet items, and fried meals also raise the risk of insulin resistance and T2DM. Fruits and vegetables that are high in nutrients, fiber, and antioxidants that protect against disease serve as a barrier to the progression of T2DM.

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According to nutritionists, foods with minimal fat, high fiber content, and a restricted number of carbs should be consumed at regular intervals (1).

Carbohydrates: Fiber consumption has been shown to have a positive impact on controlling cardiovascular risk factors, improving glycemic control, and lowering the risk of cardiovascular death in diabetics. In individuals with diabetes, fiber and whole grains should be consumed at a rate of roughly 38 grams per day for males and 25 grams per day for women.

Sucrose and Fructose: When sucrose is replaced with an iso-caloric amount of starch, it is discovered that sucrose intake of 10%–35% of total energy has no negative effects on lipid and glycemic responses. It was also reported that consuming free fructose from foods like fruits did not alter glycemic control in comparison to other sugars. Non-caloric sweeteners have a low calorific value. Hence, they don't contribute to an increase in caloric numbers, except for aspartame. They don't elevate blood sugar levels, so they're safe to eat for diabetics (32).

Proteins: These can be used to distinguish diabetes patients with and without renal damage. Protein consumption should be between 15% and 20% in those who do not have renal disease. Reduced protein consumption below the typical level in patients with kidney disease, whether micro or macro-albuminuria, has been subjected to numerous tests and meta-analyses, with no indication that low protein diets enhance glycemic management, cardiovascular risk factors, or renal disease progression. Protein consumption appears to boost insulin response in people with T2DM, hence it is not recommended to consume proteins in hypoglycemia (33).

Primary health care for diabetics

A dietician provides each diabetes patient with a personalized diet plan and is informed about the types and amounts of food that is to be consumed. Patients should eat a well-balanced diet and keep track of the number of calories they need regularly.

Exercise and physical activity are the most important strategies in the management of diabetes. Increased insulin sensitivity in tissues, improved glycemic control, better lipid profile and blood pressure, cardiovascular benefits, weight loss, a higher life quality, mental well-being, and decreased depression are all advantages of exercise (34). HbA1c levels in people with T2DM who exercised were shown to be significantly lower in some trials (35). Yoga is beneficial for the treatment of various disorders, including diabetes, hypertension, asthma, and obesity. Yoga sessions that train large body muscles to increase maximal oxygen consumption, cause a decrease in sub-maximal heart rate and increase stroke volume (36).

Treatment of diabetes

Metformin: In the absence of contraindications, it is used as the first line of treatment for T2DM. Metformin reduces fasting blood sugar levels by approximately 20% and HbA1c by approximately 1.5 %. Metformin alters the composition of gut microbiota and activates mucosal AMP-activated protein kinase (AMPK), which keeps the intestinal barrier intact. Metformin is seen to lower lipopolysaccharide levels in the circulation in the liver through this action, along with the activation of AMPK in hepatocytes. Metformin can suppress gluconeogenesis in four separate ways once it reaches the liver from the intestines (38). Metformin also functions by interacting with the Peutz-Jeghers protein LKB1, which is a tumour suppressor, and activation of AMPK via LKB1 may contribute to cell growth inhibition.

Insulin secretagogues: Sulfonylureas lower fasting plasma glucose levels, while meglitinides lower postprandial glucose levels. Sulfonylureas and meglitinides or glinides have the same mode of action, which is to stimulate insulin release by beta cells of the pancreas. They are, however, two distinct

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types of oral hypoglycemic medications. Meglitinides increase insulin release in the same way that sulfonylureas do, except for the subunit-binding site, which allows for faster absorption and stimulation of insulin secretion in meglitinides. Meglitinides, on the other hand, demand more regular doses.

Sulfonylureas are one of the most common first or second-line therapies for T2DM patients. Sulfonylureas and glinides stimulate insulin release and are regulated by ATP-sensitive potassium channels (KATP potassium channels) in the pancreatic beta-cell membrane. Although sulfonylureas and glinides bind to different receptors, they both cause a rise in cytoplasmic calcium and, as a result, insulin secretion by causing channel closure and cell depolarization. Loss of efficacy, hypoglycemia and weight gain are some of the issues associated with the usage of these medicines (39).

Alpha-glucosidase inhibitors: Acarbose, voglibose, and miglitol are the three most common alpha-glucosidase inhibitors. Acarbose is a sugar that is commonly used to treat hyperglycemia. In patients with impaired glucose tolerance, acarbose lowers the risk of cardiovascular disease and slows the progression of diabetes. The enzyme complex alpha-glucosidase hydrolyzes oligosaccharides into monosaccharides. They inhibit membrane-bound intestinal alpha-glucoside hydrolase enzymes, which are reversible. As a result, glucose absorption and digestion are delayed, resulting in lower postprandial hyperglycemia. As a result, alpha-glucosidase inhibitors do not stimulate insulin secretion as blood glucose levels are lower. Flatulence, diarrhoea, and abdominal pain are some of the negative effects (40).

Thiazolidinediones (TZD): In the United States, rosiglitazone and pioglitazone are the two most regularly utilized thiazolidinediones. TZD improves insulin sensitivity by increasing glucose consumption and decreasing glucose synthesis in muscle, adipose tissue, and the liver. By sustaining pancreatic beta-cell activity, TZD lowers blood glucose levels. Weight gain is the most common side effect.

Insulin: Insulin is the primary element in the management of all kinds of diabetes. Insulin lowers blood sugar to keep the body's blood sugar levels within a certain range. Insulin injections aid in carbohydrate metabolism, glucose storage in the liver, and glycogen conversion to fat storage. Insulin is the standard therapy for T1DM and was previously known as insulin-dependent DM or IDDM. Due to a high level of insulin resistance and/or the pancreas' declining capacity to achieve body needs, T2DM patients may additionally require insulin to achieve glucose levels (41). There are different types of insulin which can be administered such as Basal or Long-Acting Insulin, Bolus or Prandial Insulin, Premixed Insulin, Concentrated Insulin and Inhaled Insulin (42).

Conclusion

Over the last two decades, greater knowledge of T2DM pathogenesis has led to the development of injectable anti-diabetic medicines and oral medicines with better delivery mechanisms.

According to the idea of thin-fat Indian or sarcopenic obesity, Indians have an uncommonly thin-fat body composition, which leads to insulin resistance syndrome. Individuals with diabetes have a higher risk of developing a severe or critical condition, as well as a higher mortality rate, according to clinical trials of COVID-19 patients diagnosed with diabetes. In addition to pharmaceutical therapy, diabetes management includes reinforcing lifestyle adjustments such as yoga, regular exercise, stress management, and mindful eating. The National Health Service in the United Kingdom has placed a high priority on diabetes treatment which is aimed at improving the quality of life for patients. To combat the new-age diabetes pandemic in India, similar initiatives and solutions are necessary.

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Conflict of Interest

The authors declare that there is no conflict of interest in this study.

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