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Epidemiology & Programmatic Management of NCDs in India

















Highlights

- Latest data (2023) and COVID-19 concerning NCDs
- Role of frontline workers in the program
- NP-NCD updates
- Latest classifications and disease updates
- Important NCD days
- Flowcharts of Natural history of all diseases

For Undergraduates, Postgraduates, Public Health Experts & Wellness-oriented Community

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CHAPTER 3

Epidemiology of Diabetes Mellitus and its Programmatic Management in India

Seema Jain, Purushottam Giri, Bhavna Jain

Trying to manage diabetes is hard because if you do not, there are consequences you will have to deal with later in life. **Bryan Adams**

INTRODUCTION

Diabetes Mellitus (DM) is a major public health crisis at both local and global levels. It is a chronic metabolic disorder characterized by elevated levels of blood glucose, which can cause severe damage to the heart, blood vessels, eyes, kidneys, and nerves over time. Diabetes can be fatal and disabling, affecting people during their most productive years and impacting families' financial well-being and individuals' life expectancy. Diabetes is a widespread problem that affects individuals of all social classes and does not discriminate. It is a long-term illness with diverse clinical presentations and progression. Although significant progress has been made in managing diabetes over the last 150 years, diabetes complications still claim millions of lives annually, and the number of people with diabetes continues to rise. The recent global COVID-19 outbreak has been an extremely stressful experience for many individuals, and stress is a critical risk factor for diabetic patients, exacerbating glycemic control problems and leading to additional symptoms and complications.

History of Diabetes Mellitus

Diabetes, a shortened form of the term Diabetes Mellitus, is derived from the Greek word diabetes, meaning "siphon," and the Latin word mellitus, meaning "honeyed" or "sweet." The name is fitting because in diabetes, excessive sugar is present in both the blood and urine. This condition was referred to as the "pissing evil" in the 17th Century.

The term diabetes was possibly coined by Apollonius of Memphis around 250 BC, and it was first used by the Roman physician Aretaeus in the 2nd Century AD. However, references to a disease resembling diabetes can be found in much older texts from different parts of the world. The Egyptian Ebers Papyrus, dating back to 1552 BC, is the earliest known reference to a condition resembling diabetes.

The first recorded use of the term "diabete" in English dates to around 1425 in a medical text. The word "mellitus" was added to the term diabetes in 1675 by Thomas Willis because

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of the sweet taste of the urine. This sweet taste was noticed in urine by the ancient Greeks, Chinese, Egyptians, Indians, and Persians, as evidenced by their literature. The Ancient Indian medical texts of Charaka and Sushruta (400–500 BC) contain detailed descriptions of diabetes, its classification, and its management.

Definition of Diabetes Mellitus

The American Diabetes Association (ADA) defined diabetes in 1997 as "a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both." This definition has been widely adopted by other national and international organizations, including the World Health Organization (WHO).

Put simply, diabetes can be described as a metabolic and vascular syndrome with multiple causes, marked by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism due to deficiencies in insulin secretion, insulin action, or both. These deficiencies can lead to changes in both small blood vessels (microangiopathy) and large blood vessels (macroangiopathy).

Classification of Diabetes Mellitus (Fig. 3.1)

Diabetes cases can generally be classified into two main categories—polygenic forms and monogenic forms. While less common forms of diabetes may exist, such as those that are genetically determined or associated with other medical conditions or drugs.

Polygenic diabetes: Meaning they are related to a change, or defect, in multiple genes. It can be broadly classified into **two categories**: Type 1 diabetes mellitus **(T1DM)** and Type 2 diabetes mellitus **(T2DM)**. Also includes **Prediabetes, Gestational diabetes (GDM) and LADA.**

Type 1 diabetes mellitus (T1DM): also called **"**Immune mediated" or "insulin dependent diabetes" or "juvenile-onset diabetes" accounts for 5–10% of diabetes. It is a genetic condition that often shows up early in life mainly in children, teens, and young adults. It is due to cellular

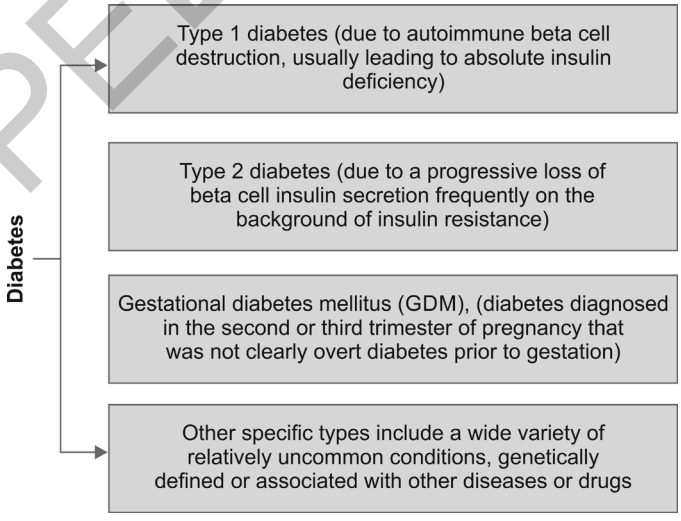

Fig. 3.1: Classification of diabetes mellitus.

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mediated autoimmune destruction of pancreatic beta cell (type 1A) with consequent insulin deficiency, which is prone to ketoacidosis. In this type of diabetes, the immune system mistakes the body's own healthy cells for foreign invaders. The immune system attacks and destroys the insulin-producing beta cells in the pancreas. After these beta cells are destroyed, the body is unable to produce insulin. The assessment of this type of diabetes includes additional tests for the presence of one or more of the following:

- Islet cell autoantibodies
- Autoantibodies to GAD (GAD 65)
- Insulin (as manifested by low or undetectable levels of plasma C-peptide)
- Tyrosine phosphatase IA-2 and IA-2b, and ZnT8
- Human leukocyte antigen (HLA) associations with linkage to the DQA and DQB genes

Type 2 diabetes mellitus (T2DM): Type 2 diabetes, which was formerly known as "non-insulin dependent diabetes" or "adult-onset diabetes," makes up 90–95% of all cases of diabetes. This type of diabetes is primarily associated with an unhealthy lifestyle and develops gradually over time. It can manifest as insulin resistance with some insulin deficiency, or as a secretory defect with insulin resistance, although ketosis is less common. In response to the insulin resistance, the pancreas of a person with type 2 diabetes will often produce more insulin in an attempt to compensate. However, the body cannot properly utilize insulin, leading to an accumulation of glucose in the bloodstream.

Prediabetes: Prediabetes occurs when the level of glucose in the blood is elevated but not high enough to be classified as diabetes. This term is commonly used to refer to individuals with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or a glycated hemoglobin (A1C) level of 5.7% to 6.4%. People with prediabetes are at an increased risk of developing type 2 diabetes and its associated complications, as well as heart disease and stroke. The Centers for Disease Control and Prevention (CDC) recommends lifestyle changes for those with prediabetes to reduce their risk of developing type 2 diabetes. Making healthy lifestyle choices can help reverse prediabetes.

Gestational diabetes mellitus (GDM): Gestational diabetes (GDM) is a condition where high blood sugar is first diagnosed during pregnancy in women who did not previously have diabetes, or it can refer to glucose intolerance that is first recognized during pregnancy. Typically, GDM is identified between the 24th and 28th week of pregnancy. Similar to other types of diabetes, GDM affects the way your body processes glucose, which can impact the health of the baby and the pregnancy. Although GDM usually resolves after the birth of the baby, it can increase the risk of developing type 2 diabetes later in life for the mother. Additionally, the baby is more likely to have obesity as a child or teen and to develop type 2 diabetes later in life.

Latent autoimmune diabetes in adults (LADA): LADA is a slow-progressing form of autoimmune diabetes. Like the autoimmune disease type 1 diabetes, LADA occurs because your pancreas stops producing adequate insulin, most likely from some "insult" that slowly damages the insulin-producing cells in the pancreas. But unlike type 1 diabetes, with LADA, you often would not need insulin for several months up to years after you have been diagnosed.

Monogenic diabetes: Some rare forms of diabetes result from mutations or changes in a single gene and are called monogenic. It includes **MODY** and **Neonatal Diabetes**.

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Maturity-onset diabetes of young (MODY): Maturity-Onset Diabetes of the Young (MODY) is a rare form of diabetes that differs from both type 1 and type 2 diabetes and has a strong familial link. It typically develops during adolescence or early adulthood. MODY is caused by a mutation in a single gene, and if a parent carries this mutation, there is a 50% chance of passing it down to their child. Individuals who inherit the mutation will generally develop MODY before the age of 25, regardless of their lifestyle, weight, or ethnic group.

The key features of MODY are:

- Being diagnosed with diabetes under the age of 25.
- Having a parent with diabetes, with diabetes in two or more generations.
- Not necessarily needing insulin.
- Most common types of MODY are HNF1-alpha (accounts for 70%), HNF4-alpha, HNF1-beta, glucokinase.

Neonatal diabetes mellitus (NDM): NDM is a rare form of diabetes that typically occurs within the first 6 months of life, and it is often initially misdiagnosed as type 1 diabetes, which is more common in children over 6 months of age. Approximately half of the infants diagnosed with NDM have a lifelong condition known as Permanent Neonatal Diabetes Mellitus, while the other half have a transient form that resolves within the first 12 weeks of life but may recur later. Fetuses with NDM often have intrauterine growth restriction, leading to smaller newborns relative to their gestational age.

Problem Statement: Extent of Problem

Diabetes is an iceberg disease. Although increase in incidence and prevalence have occurred globally but dramatic rise has occurred in societies with economic transition.

Global Prevalence of Diabetes

Diabetes mellitus is a significant cause of mortality and reduced life expectancy, and it represents one of the most substantial public health concerns worldwide. The disease imposes a considerable burden on global public health as well as socioeconomic development. While there have been reports of declining incidence rates in some countries, the prevalence of diabetes has been on the rise over the past few decades in most developed and developing nations.

According to WHO, 2020

- In 1980, 108 million people worldwide had diabetes. By 2014, that number had risen to 422 million.
- In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths and 48% of all deaths due to diabetes occurred before the age of 70 years, thus becoming the ninth leading cause of death globally. By the year 2035, nearly 592 million people are predicted to die of diabetes.
- Between 2000 and 2016, there was a 5% increase in premature mortality rates (i.e., before the age of 70) from diabetes.

According to IDF Diabetes Atlas Tenth Edition, 2021

- 537 million adults are now living with diabetes worldwide a rise of 16% (74 million) since the previous IDF estimates in 2019. The total number of people living with diabetes is projected to rise to 643 million by 2030 and 783 million (or one in eight adults) by 2045 which is 51% increase from 2019.

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- Global prevalence of diabetes has reached 10.5%, with almost half (44.7%) of adults undiagnosed.
- 3 in 4 adults with diabetes live in low- and middle-income countries. Almost 1 in 2 (240 million) adults living with diabetes are undiagnosed.
- Diabetes caused 6.7 million deaths. Diabetes caused at least USD 966 billion dollars in health expenditure—9% of total spending on adults.
- More than 1.2 million children and adolescents (0–19 years) are living with type 1 diabetes
- 1 in 6 live births (21 million) are affected by diabetes during pregnancy
- China has the highest number of diabetes accounts worldwide, with 116 million people with diabetes. Following China is India (77 million people with diabetes) and then the United States (31 million people with diabetes).

The Indian Scenario

Over the last thirty years, the prevalence of diabetes in India has been steadily rising, with the country now accounting for a significant portion of the global burden. Furthermore, there has been a substantial increase in the incidence of prediabetes and undiagnosed diabetes. The rise in type 2 diabetes mellitus, particularly among younger age groups, is a growing public health concern. Epidemiological transition has led to a shift in India's disease patterns, with communicable, maternal, neonatal, and nutritional diseases (CMNNDs) contributing significantly to reduced mortality while noncommunicable diseases (NCDs) and injuries have become more prominent.

- The prevalence of diabetes in India has risen from 7.1% in 2009 to 8.9% in 2019. India ranks second after China in the global diabetes epidemic with 77 million people with diabetes.
- Of these, 12.1 million are aged >65 years, which is estimated to increase to 27.5 million in the year 2045. It is also estimated that nearly 57% of adults with diabetes are undiagnosed in India, which is approximately 43.9 million.
- Diabetes contributed to 3.1% of total deaths in India, with slight variation among men 2.9% and woman 3.5%. The crude death rate due to diabetes increased in India from 1990 to 2016 by 13.1% from 10 to 23.1 per 1,00,000 population. Of total deaths due to diabetes in 2016, 42.6% were in people younger than 70 years.
- In India, diabetes accounted for 2.2% of the total disability-adjusted life years (DALYs) in 2016. Of the diabetes-related DALYs in that year, 57.2% were due to years of lost life (YLLs) and 42.8% were due to years lost to disability (YLDs). Recent research has shown that both urban and rural areas are experiencing a rapid increase in the burden of diabetes. Type 2 diabetes (T2DM) has been steadily rising in India since the 1990s, and more rapidly since the year 2000. According to the WHO-ICMR NCD list, a study was conducted among 44,523 individuals aged 15–64 years between 2003 and 2005 in urban and rural areas of six different states, which revealed a self-reported diabetes prevalence of 4.5%.

COVID-19 AND DIABETES

COVID-19, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the most significant pandemic in the last century, affecting humanity globally. The pandemic has caused stress and disrupted lives due to its rapid spread and high mortality rate. Studies have identified type 2 diabetes, hypertension, cardiovascular diseases, obesity, and chronic kidney disease as the most common comorbidities associated with SARS-CoV-2 infection.

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These conditions are associated with worse outcomes, including mortality. Diabetes mellitus (DM) is a chronic, progressive disease that is considered the largest global health problem in the twenty-first century. For diabetic patients, stress is a major risk factor that can worsen glycemic control, leading to more symptoms and complications.

The relationship between COVID-19 and DM is complicated and bidirectional

Diabetes mellitus (DM) is considered one of the most important risk factors for a severe course of COVID-19. Several factors present in DM may contribute to this risk, including older age, a proinflammatory and hypercoagulable state, weaker immune system, less viral clearance rate, hyperglycemia, and underlying comorbidities. There may be potential pathogenetic links between COVID-19 and diabetes, including inflammation, effects on glucose homeostasis, hemoglobin deoxygenation, altered immune status, and activation of the renin-angiotensin-aldosterone system (RAAS).

- Increased risk of adverse infection outcomes (severe disease, ICU admission, need for assisted ventilation and mortality), even at levels of hyperglycemia lower than those suggestive of diabetes.
- Increased risk of "long COVID" (tiredness, breathlessness, muscle and joint pain, inability to focus)

On the other hand, a severe COVID-19 infection, and its treatment with steroids, can have a specific negative impact on non-diabetic and diabetics.

- Increased risk of development of new-onset hyperglycemia in infected individuals
- Worsening of glycemic control in pre-existing diabetes through increased insulin resistance and reduced β-cell secretory function.
- Stress hyperglycemia—during course of illness COVID-19 can trigger excessive stress and high secretion of hyperglycemia-related hormones, such as catecholamine and glucocorticoid leading to irregular variability of glucose in blood and increase blood-glucose.

Treatment

- During the COVID-19, tight control of glucose levels and prevention of diabetes complications is necessary to keep susceptibility low and to prevent severe course of disease.
- Screen every patient at admission for hyperglycemia with at least two capillary blood glucose values (1 pre-meal and 1 post-meal value) by a glucometer.
- As COVID-19 lacks definitive treatment so far, patients with diabetes mellitus should follow general preventive rules strictly and monitor glucose levels more frequently, engage in physical activity, eat healthily (start diabetic diet strictly adhering to quantity and timing) and control other risk factors.

Pharmacotherapy

- **Treatment of patients with known diabetes who are on OAD at admission**
  - To continue existing OAD if all of the below-mentioned criteria are fulfilled:
    - BG levels are controlled (Pre-meal <140 mg/dL and post-meal <180 mg/dL)
    - Patient is conscious, oriented and has good oral acceptance
    - COVID symptoms are mild
    - KFT and LFT are normal
  - If above criteria not fulfilled consult endocrinologist/physician to start insulin.

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- **To initiate OAD in patients newly detected to have diabetes at admission**
  (At admission: pre-meal BG: 150 to 180 mg/dL and/or post-meal BG 200 to 250 mg/dL)
  - Consult endocrinologist/physician at earliest to initiate or optimize OAD
  - If there is a delay in consulting endocrinologist/physician, initiate on Tab Metformin 500 mg BD and a Gliptin (Tab Vildagliptin 50 mg BD or Tab Sitagliptin 100 mg OD).
  - If BG levels at admission are above the range mentioned (pre-meal ≥180 mg/dL or post-meal blood glucose ≥250 mg/dL) → start on insulin.
  - Do not initiate drugs, such as pioglitazone and SGLT2 inhibitors in patients with COVID
- **To initiate insulin for patients newly detected with diabetes**
  Indication: At admission: pre-meal BG: ≥180 mg/dL or post-meal BG ≥250 mg/dL

Epidemiology of Diabetes Mellitus

The global diabetes epidemic can largely be attributed to rapid transitions in social structures, economics, nutrition, and lifestyle in developing countries. Several socio-demographic factors are thought to contribute to the occurrence of diabetes.

Aging

Over the next five decades, the global population is expected to rapidly age due to an increase in life expectancy and a decline in fertility. The prevalence of diabetes is known to increase with age, and in developed economies, it typically occurs in individuals aged 65 years and above. However, in India, earlier studies have reported that the onset of diabetes occurs in a younger age group of 45–65 years. A study conducted in Chennai, South India, known as CURIS, reported that younger age groups were more frequently affected by diabetes. Around 5% of individuals aged 25–34 years had diabetes, compared to over 20% of those aged 40–49 years.

Urbanization

The rising rates of diabetes in both urban and rural areas of India suggest that urbanization is a significant contributing factor to the incidence of diabetes and other noncommunicable diseases (NCDs). Urbanization, which includes both urban expansion into rural areas and migration from rural to urban areas, plays a crucial role in the diabetes epidemic. The prevalence of diabetes in urban areas, according to the ICMR-INDIAB study, was twice that of rural areas, with 11.2% of urban populations affected compared to 5.2% of rural populations.

Family History of Diabetes

If you have a family health history of diabetes, you are more likely to have prediabetes and develop diabetes.

Socioeconomic Status

The ICMR-INDIAB study revealed that there is a correlation between a state's per capita GDP and the prevalence of diabetes. For example, Chandigarh, which has the highest GDP of $3,433, had a prevalence of 13.6%, while Bihar, the state with the lowest GDP of $682, had a prevalence of 4.3%. Additionally, the study identified socioeconomic disparities as a possible factor contributing to the increase in diabetes prevalence, particularly among individuals with low socioeconomic status in urban areas. The study suggests that diabetes will likely have a greater impact on the poorer segments of Indian society, which reflects the future of the disease in a rapidly growing economy, such as India.

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Physical Inactivity

The detrimental impact of insufficient physical activity on public health is a major concern. Eliminating physical inactivity could prevent 6–10% of major noncommunicable diseases, such as coronary heart disease, type 2 diabetes, and breast and colon cancers, while also increasing life expectancy. In underdeveloped nations, where individuals were primarily engaged in unmechanized agricultural activities, occupational physical activity levels were traditionally high, and the lack of recreational physical activity did not have a significant impact on overall physical activity levels. However, recent years have witnessed a substantial decrease in overall physical activity levels, which may be attributed to the transition towards industrialization and mechanization. As a result, the workforce has shifted away from physically demanding agricultural occupations and towards sedentary occupations.

Dietary Factors

In many regions of the world, economic growth has been accompanied by a rapid "nutrition transition," which involves significant changes in dietary and food consumption patterns. Traditional diets typically consisted of high-fiber foods with a low glycemic index and low glycemic load due to the consumption of coarse whole grains. However, with increased affluence and the availability of modern food processing technologies, there has been a shift away from whole grains to polished cereals. In addition, diets have become higher in fats and oils, including trans-fats, as well as meat and animal products, while fiber, fruits, and vegetables are consumed in lower quantities. Research indicates that increased intake of fruits and vegetables, whole grains, low-fat dairy products, low glycemic load, and plant-based diets are associated with a lower risk of developing type 2 diabetes. Conversely, studies have linked diets with high intake of refined grains, processed meats, and added sugars, as well as low-fiber diets, to an increased risk of type 2 diabetes.

Others

- Being overweight/obese (BMI is >23 kg/m^2)
- Hypertension
- High levels of harmful blood fats/Hyperlipidemia—triglyceride and/or cholesterol levels are higher than normal
- Addictions, such as tobacco use, drugs and harmful use of alcohol
- Women with polycystic ovarian syndrome
- Stress and depression

Signs and symptoms of Diabetes Mellitus

- Frequent urination
- Increased hunger
- Excessive thirst
- Unexplained weight loss
- Lack of energy, extreme tiredness
- Lack of interest and concentration
- Blurred vision
- Repeated or severe infections, such as vaginal infections
- Slow healing of wounds, dry or itchy skin
- Impotence in men

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The clinical triad of T2DM includes polydipsia, polyuria and weight loss. Polyphagia though common is not included in clinical triad.

Pathophysiology and Metabolism in Diabetes

Beta cells are present in the islets of Langerhans or responsible for secretion of insulin.

Islets of Langerhans

Islets, or small clusters of cells, are often referred to as "micro-organs" because they play an important role in regulating blood glucose levels. In healthy adult humans, there are approximately one million islets distributed throughout the pancreas. These islets consist of various types of cells, including Alpha, Beta, and Gamma cells, each of which performs distinct physiological functions.

Islets in T1DM: Beta cell destruction with absolute insulin deficiency. Further classified into two types:

1. *Autoimmune:* Insulin deficiency is due to an autoimmune mediated selective destruction of beta cells, also there is role of environmental factors and genetic susceptibility. Islet cell reactive autoantibodies are identified in the serum of patients with T1DM.
2. *Idiopathic:* No autoantibodies or insulitis. Fulminant disorder, remarkably abrupt onset and high serum concentration of pancreatic enzymes. Pancreatic biopsy shows T-cell predominant infiltrates in exocrine pancreas.
   Some diabetic cases are also seen as an event secondary to hereditary pancreatitis.
   Clinically, type-1 diabetes is combination of hyperglycemia, variable loss of C peptide secretion and dependence on exogenous insulin for survival.

Islets in T2DM: Type 2 diabetes mellitus (T2DM) is a condition where beta cells, which produce insulin, can be damaged by overuse or by the buildup of a protein called insulin amyloid polypeptide (IAPP). T2DM typically arises from a combination of insulin resistance and defects in insulin secretion, often accompanied by high levels of glucagon. The severity of T2DM can range from predominantly insulin resistance to predominantly insulin secretion defects, resulting in relative insulin deficiency.

Islets in GDM: Insulin resistance is a common occurrence during the second trimester of pregnancy, and it may progress to type 2 diabetes mellitus (T2DM) after delivery. Women with multiple pregnancies are at a higher risk of developing diabetes in subsequent pregnancies. In gestational diabetes mellitus (GDM), the pancreas may show islet hypertrophy, inflammation of large islets, and intracellular fibrosis. Over time, diabetes can lead to a decrease in pancreatic volume, an increase in fat percentage, and lower fat density.

Overview of Insulin and Its Functions

Insulin is a peptide hormone consist of two polypeptide chains linked to each other by two disulfide bonds. The A and B chains 21 and 30 amino acids respectively.

Insulin Receptor

Insulin plays a major role via acting on various insulin receptors present all over the body, one of these receptors is GLUT-4 type which is present in the skeletal muscles, fat cells.

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Insulin stimulates translocation from cytosol to cell membranes. Structurally insulin receptor has two alpha and two beta subunits, via which insulin mediates its action.

Example: Phosphatidylinositol-3-kinase (PI3K) Pathway stimulates the translocation of GLUT-4 to cell surface. PI3K is also involved in synthesis of glycogen proteins and lipids, also in expression of various genes. Distribution of various IRS proteins varies in different tissues and hence the effect of insulin is different in different tissues. Defect in post-receptor pathways is thought to be responsible for insulin resistant state and Type 2 DM.

Role of Insulin

Muscles: GLUT-4 is a protein responsible for glucose uptake in muscle cells. During a well-fed state, it promotes glycogen and protein synthesis. In the absence of insulin, muscle catabolism occurs, leading to the release of amino acids that can be used for gluconeogenesis. During starvation, low insulin levels can lead to reduced protein synthesis, resulting in the loss of lean body mass.

Adipose tissue: Glucose enters fat cells through a process that is dependent on GLUT-4. When the body is in a well-fed state, insulin promotes the creation of fat (lipogenesis) while simultaneously inhibiting the breakdown of fat (lipolysis). During periods of starvation, lipolysis is triggered, causing adipocytes to release free fatty acids (FFAs) into circulation for use by the heart. If insulin is not present, the liver converts FFAs into ketone bodies which can serve as an alternative energy source for the brain.

Liver: In well fed state, glycogen and protein synthesis is stimulated while gluconeogenesis and ketone productivity is suppressed by insulin. In insulin deficiency, there is unrestricted glycogenolysis and gluconeogenesis, leading to increased hepatic glucose output into the circulation.

Brain: Insulin acts as neuropeptide involved in appetite regulation. In well fed state, glucose is the primary product for metabolism accepted via GLUT-3 receptor which is insulin independent, but may function on ketone bodies as an alternative in starvation state.

Kidney: The enzyme systems for gluconeogenesis and glycogenolysis or present in kidney and are regulated by insulin in the same manner as in liver. Kidneys contribute to 10 to 20% of total glucose influx into circulation during fasting state.

Metabolism in Diabetes

Carbohydrate metabolism: The hallmark of diabetes mellitus is metabolic derangement resulting from—relative insulin deficiency, insulin resistance and glucagon excess.

- Due to insulin deficiency entry of glucose into the cells (adipocyte and muscle) is hampered.
- The excess amount of glucagon relative to insulin causes decrease in amount of fructose-2-6-bisphosphate in the liver, resulting in inhibition of glycolysis and stimulation of gluconeogenesis.

Insulin resistance: It is subnormal glucose response to endogenous and/or exogenous response.

Caused by

- Obesity
- Stress induced (excess counter hormones, such as GH (Growth hormone), cortisol, Catecholamines and glucagon.

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- Medication (Glucocorticoids), viral (HIV)
- Pregnancy (placental lactogen)
- Lipodystrophy
- Insulin antibodies (anti-insulin and anti-insulin receptor antibody)

Elevated glucose levels beyond the normal range can occur in diabetes. In severe cases, blood glucose levels may remain above the renal threshold of 126 mg/dL throughout the day, leading to glycosuria, the presence of glucose in the urine. Polyuria, or excessive urination, occurs as water is excreted along with the glucose, which can lead to thirst, a common symptom of diabetes. In addition, diabetes can significantly reduce the conversion of glucose into fatty acids through acetyl-CoA.

Protein metabolism: Transport and update of amino acids in the peripheral tissue are decreased in diabetes causing an elevated level of circulating among acids, particularly alanine which enhances gluconeogenesis in the liver. Breakdown of amino acids during gluconeogenesis results in increased production of urea.

Lipid metabolism: In diabetes, increased lipolysis leads to the hydrolysis of stored lipids, which releases free fatty acids (FFAs) into circulation. These FFAs inhibit the synthesis of new fatty acids in the liver by inhibiting acetyl-CoA carboxylase. Instead, the excess acetyl-CoA is used for the synthesis of ketone bodies, which are then used by the heart and skeletal muscles for energy production. The normal range of ketone bodies in the blood is 1 mg/dL, but when the serum levels rise above 5 mg/dL, they appear in the urine. The loss of ketone bodies in the urine depletes the alkali reserve and can cause the pH of blood to drop as low as 7.0 in severe cases.

In diabetes, gluconeogenesis from amino acids is increased, while the synthesis of fatty acids from glucose is inhibited, indicating altered metabolism. In severe cases of diabetes, blood glucose levels can rise up to 500 mg/dL, which leads to increased glucose uptake by tissues. Despite this abundance of glucose, the body is unable to use it efficiently, and instead shifts to using fat for energy, resulting in a state of "starvation in the midst of plenty." The constant loss of glucose in the urine can cause constant hunger and weight loss, as the body's fat stores are depleted due to increased breakdown and decreased synthesis. Excess glycogen deposits can also be found in the renal tubules (Armani-Ebstein lesions), likely due to gluconeogenesis. Increased concentrations of sorbitol in the lens, nerves, and cerebrospinal fluid (CSF) of diabetic patients have been implicated in the development of cataracts and neuropathy.

Diagnostic Criteria of Diabetes Mellitus

Diabetes is a group of metabolic disorders characterized by high levels of glucose in the blood due to defects in insulin secretion, insulin action, or both. The chronic hyperglycemia associated with diabetes can lead to long-term damage, dysfunction, and failure of various organs, including the eyes, kidneys, nerves, heart, and blood vessels. In patients with diabetes, insulin action on target tissues is reduced, resulting in altered metabolism of carbohydrates, fats, and proteins. The primary cause of hyperglycemia can be challenging to identify since deficiencies in insulin secretion and defects in insulin action often coexist in the same patient.

Diagnosis of DM

The diagnostic criteria by WHO and ADA is widely used for diagnosis of DM.

- **Symptomatic subjects:** A patient presenting with classic symptoms of diabetes, such as polyurea, polydipsia, unexplained weight loss and has a random plasma glucose level of more than or equal to 200 mg/dL is sufficient criteria for diagnosis of diabetes.

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- **Asymptomatic subjects**: Diagnosis can be established by—
  - Fasting plasma glucose values ≥ 126 mg/dL. (Fasting is defined as no caloric intake for at least 8 hours).
  - Two-hour plasma glucose values of ≥ 200 mg/dL during an oral glucose tolerance test (OGTT). The test should be performed as described by WHO, using glucose load containing the equivalent of 75 grams anhydrous glucose dissolved in water.
  - Hemoglobin A1c (HbA1c) values more than or equal to 6.5%. Diabetes control and complications trial (DCCT) assay.

Diagnosis of Prediabetes

When the plasma glucose is above normal value but not high enough to diagnose diabetes, it could be prediabetic state. This would be present as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

- Impaired glucose tolerance is defined as fasting plasma glucose (FPG) <126 mg/dL (7 mmol/L), a 2-hour post-OGTT ≥140 mg/dL (7.8 mmol/L) but <200 mg/dL (11.05 mmol/L).
- Impaired fasting glucose is defined as 100–125 mg/dL (6.1. To 6.9 mmol)
- HbA1c levels more than 5.7% but <6.4%.

Diagnosis of GDM

American College of Obstetricians and Gynecologists (ACOG-2017) stated it as a disorder of carbohydrate intolerance with onset or first recognition during pregnancy, and that clinicians may consider one elevated value as diagnostic of positive test via OGTT as per DIPSI criteria (2004). **Figure 3.2** shows the cut-off plasma glucose values for gestational diabetes mellitus.

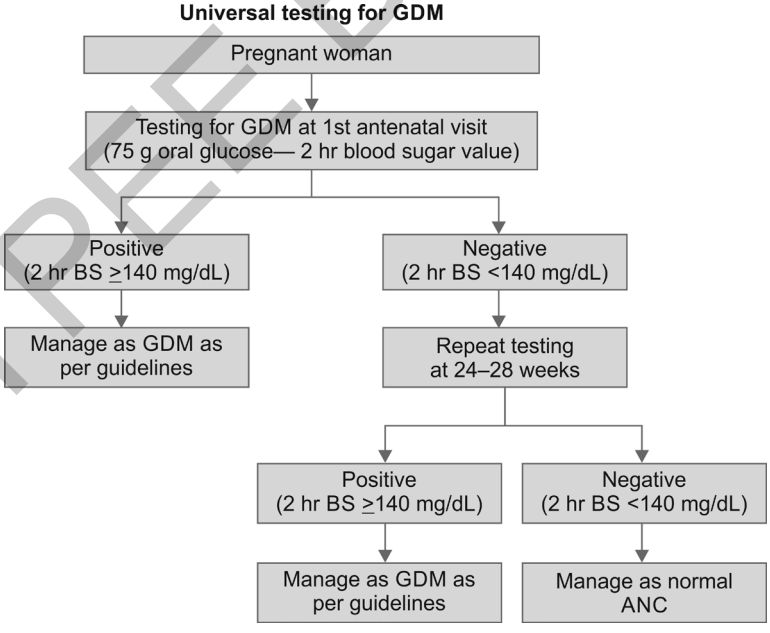

Fig. 3.2: Cut off values for GDM.

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Epidemiology & Programmatic Management of NCDs in India

This book on epidemiology is an attempt to throw more light of knowledge on non-communicable diseases especially amongst budding postgraduate students of community medicine, public health experts and also community nurses working in various set-ups. From my experiences in the past, I have felt the growing need for a book which could throw light on diagnosis, care and control of different lifestyle diseases, problems related to elderly age, etc., in a comprehensive way. The community medicine specialists, wellness physician, chronic disease specialist, fitness trainers are required to know about lifestyle diseases. These can be seen in every household globally and therefore its line of management must be known. Through this book, we have tried to throw light on various levels of preventive measures and the national programs related to the disease. We hope that reading this book will add more value to people's lives by adding more quality years in disease cycle.

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