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A Systematic Review: Clinical Manifestations of Diabetes Mellitus and The Role of Pharmacists in Management of Type II Diabetes

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Abstract

Diabetes mellitus is a condition in which the metabolism of carbohydrates, proteins, and lipids is disrupted owing to reduced insulin production, increased glucagon secretion, and the development of insulin resistance in body cells. The prevalence of diabetes in Pakistan varies based on age, gender, and geography. Genetic, behavioral, and environmental factors contribute to the development of type II diabetes. Insulin resistance by the cells and a decreased or inadequate quantity of insulin produced by the beta cells of the pancreas result in type II diabetes, which is characterized by high amounts of proinflammatory cytokines and free fatty acids in plasma. In diabetic individuals, the imbalance between insulin and glucagon production results in an increased amount of glucagon in the blood and hyperglycemia. Insulin resistance develops in response to physical inactivity, steroid use and a high-calorie diet. Glucagon and glucose-dependent insulinotropic polypeptide (GIP) levels also rise. Major consequences of diabetes include diabetic retinopathy, neuropathy, vasculopathy, end-stage renal disease, cardiovascular disease, and stroke. In this review medical therapy including the role of insulin in the management of DM 2 will be discussed. The role of pharmacists in its management will also be focused since tailored patient education is more effective than group sessions in addressing poorly managed diabetes. Among the non-pharmacologic parts of diabetes treatment is teaching patients about the advantages of a healthy diet as well as regular physical activity. In treating type 2 diabetes, bariatric surgery is more effective than medication. Depending on the patient's state, anti-diabetic drugs may either lower insulin resistance or boost insulin secretion.

Keywords Diabetes Mellitus, Insulin-Dependent Diabetes Mellitus, Non-Insulin-Dependent Diabetes Mellitus

1. Introduction

Diabetes mellitus is a disorder in which the metabolism of carbohydrates, proteins, and fats is impaired (1), which results from the following factors: decreased secretion of insulin, increased secretion of glucagon, and decreased responsiveness of body cells to insulin. Thus the cause of diabetes is multifactorial, which ultimately primes hyperglycemia, hence leading to many types of physiological dysfunctions that sprawl from microvascular (renal, retinal, and neuropathic) to macrovascular (peripheral vascular disease, coronary artery disease). Neuropathy, thus caused by diabetes

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mellitus, will compromise both the peripheral and autonomic nervous systems.

Type II DM differs from type I DM in that the secretion of insulin is reduced and patients do not have complete dependency on insulin while in type I, patients are fully dependent on insulin (2).

In the past, it was considered that type II DM mainly affected people who were older than 40, but recent data shows that it can also affect children of a younger age. Such children have a familial background of DM. Astonishingly, the occurrence of type II DM in children has outnumbered the cases of type I DM.

This chronic disease can be handled with long-term medical attention; otherwise, the above-mentioned complications will devastate the life of a diabetic patient. DM produces economic constraints on the individual because the medical expenditure would be 2.3 times greater than for non-diabetic patients (3).

2. Epidemiology

2.1. Worldwide

The world is on the verge of having more diabetic patients; as predicted by the International Diabetes Federation (IDF) in 2011, when the diabetic patients were 366 million, while, in 2030 the diabetic population will be 552 million (4). In Asia, countries like India, China, Indonesia, Japan, Pakistan, Russia, and Bangladesh; and in America, the United States of America, Brazil, Europe, and Italy are the top 10 countries in the world that have more diabetic patients. On the other hand, in the coming 20 years, the percentage of diabetic patients in Africa will increase to a greater extent (5).

2.2. Pakistan

Several factors affect the prevalence of diabetes: age, gender, and place (6). According to a study in 2004, the prevalence percentage of diabetes in Pakistan was 7.6–11 percent (7) which has increased to 11.7% according to study conducted in 2016.While the province-wise prevalence of type II DM in females and males is given in the following table and chart,

Table 1: Prevalence of type II DM in Pakistan

Province	Mean prevalence in Females	Mean prevalence in males
Sindh	11.70%	16.20%
Punjab	9.83%	12.14%
Baluchistan	8.90%	13.30%

Overall, the prevalence in males was 11.20 percent, which was higher than the prevalence in females, which was 9.19 percent. In addition, the prevalence of plebeians was 14.81 percent in urban regions and 10.34 percent in rural areas (8).

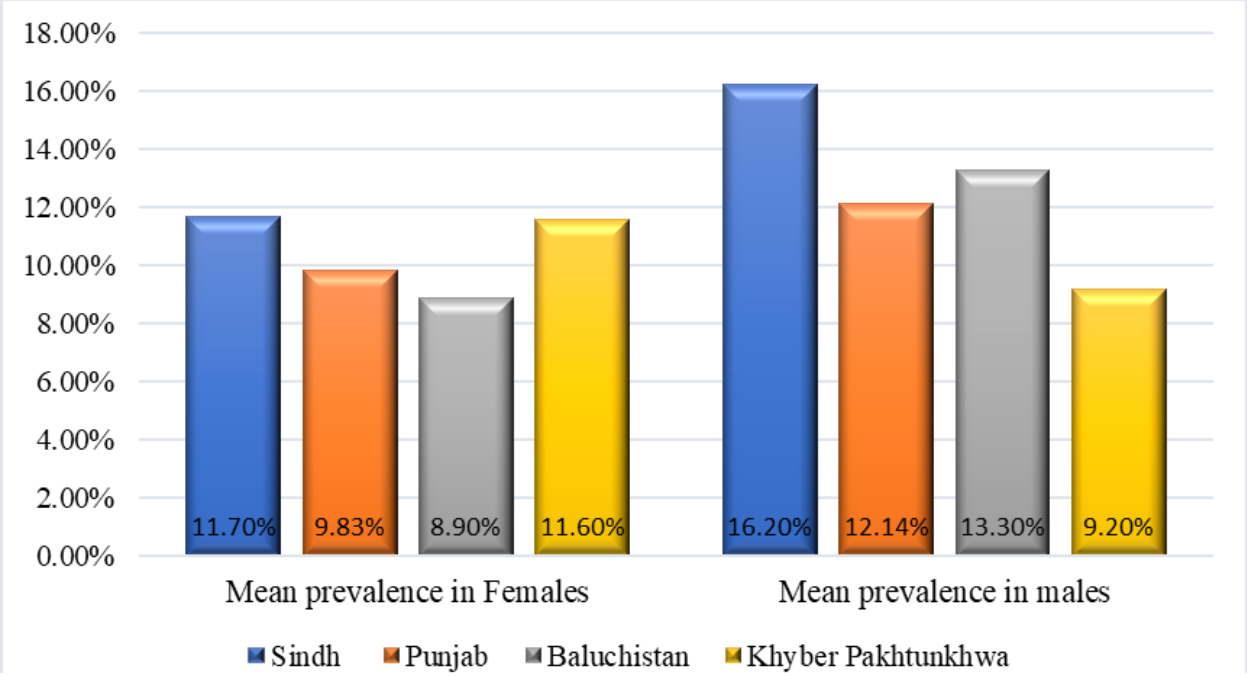

Figure 1: Prevalence of type II DM in Pakistan

3. Etiology

Certain factors predispose the type II DM:

- Genetic factors, lifestyle, high-carb diet, and Obesity (9).
- Higher body mass index.
- Conditions like hypertension, prehypertension (10), Cushing syndrome, acromegaly, and pheochromocytoma.
- Environmental pollutants (11).

4. Risk Factors

The following are the core risk factors for type II DM:

Table 2: Risk Factors Associated with Type II DM

Risk factor	Comment
Age	> 45 years
Weight	> 120% of than desired body weight
Family history	First-degree relatives e.g. parents or siblings
Hx of Impaired glucose tolerance	or the history of impaired fasting glucose
Hypertension	> 140/90 mmHg
Dyslipidemia	HDL level < 40mg/dL or TGs level > 150mg/dL
Hx of gestational diabetes mellitus	Or delivering a baby with ≥ 9lb weight
Polycystic ovarian syndrome	This syndrome results in insulin resistance

5. Genetic Influences

Due to the complexity of the genetics of type II DM, it is difficult to understand its genetic basis. However, certain genes are responsible for the destruction of beta cells and insulin resistance. Among the various genetic variants, the transcription factor 7-like 2 (TCF7L2) gene has the strongest predisposition for type II DM (12).

6. Depression

There is enough evidence that depression is a significant risk factor for type II DM. According to Pan et al., women with depression are more at risk for developing diabetes (13).

7. Preeclampsia and Gestational Hypertension

A retrospective cohort study of 1,010,068 pregnant females has found that the occurrence of gestational hypertension and preeclampsia would lead to the development of diabetes mellitus after delivery. And the risk is further enhanced when such pregnant females have gestational diabetes along with preeclampsia and gestational hypertension (14).

8. Pathophysiology

As mentioned earlier, type II DM is characterized by insulin resistance by the cells and a reduced or insufficient amount of insulin released by the beta cells of the pancreas. A question arises about why the cells become resistant to insulin. The answer is an elevation in levels of proinflammatory cytokines and free fatty acids in plasma. The insulin resistance makes the cells hungry for glucose; this gives a pseudo-signal to the liver and adipose tissues of a decreased level of glucose in the blood, which, by receiving this false signal, starts the production of glucose from glycogen in the liver and the production of a precursor of glucose from the breakdown of fats in adipose tissues, respectively.

In addition, the balance between insulin and glucagon secretion is also disrupted, as glucagon-producing cells are normal while insulin-producing cells are abnormal. The whole situation would lead to an enhanced level of glucagon in the blood, which primes hyperglycemia (15). Interestingly, in the presence of type II DM, there must be a coexistence of both diminished insulin production and insulin resistance. This statement can be elaborated with an example of obese people: all obese people have insulin resistance, but type II DM only preys on those whose insulin production is insufficient to meet the demand. Chronic diabetes might also result in atrophy of the pancreas. (16)

9. Beta-Cell Dysfunction

In diabetic patients, the first thing that unnoticeably occurs when they are normal is the dysfunction of beta cells. So, this dysfunction develops earlier, and it is not necessary that it occur after the stage of insulin resistance. This finding has given an option for the treatment of beta cells before the actual disease manifests.

10. Insulin Resistance

The first thing that occurs in the progression of abnormalities towards glucose intolerance in diabetic patients is the elevation of glucose levels after meals. In the second stage, due to failure in the stoppage of gluconeogenesis from the liver, a higher fasting glucose level in the blood also develops. Insulin resistance occurs with physical inactivity, steroid administration, and a high-calorie diet. Besides, during the induction process of such resistance, the levels of glucagon and glucose-dependent insulinotropic polypeptide (GIP) also increase with hyperglycemia (17).

11. Signs and Symptoms

Many patients of type II DM show no symptoms, so their disease remains hidden for many years; eventually, they remain undiagnosed in that occult period of the disease. And when such patients are diagnosed, as stated in previous studies, 4–7 years have passed. The classic symptoms of diabetes mellitus are polyuria, polydipsia, polyphagia, and weight loss. Other symptoms could include blurred vision, lower extremity paresthesia, and yeast infection (balanitis in males) (18).

12. Diabetic Complications (Diabetes-associated mortality and morbidity)

Diabetes causes morbidity and mortality in diabetic patients because it affects the heart, kidneys, eyes, and nervous system (19). In most deaths, diabetes plays a contributing role, but unfortunately, such cases are not frequently reported. In the clincher, diabetic patients are two times more prone to death as compared to normal individuals (20). According to a perspective on the diabetes study conducted in the UK, the following were the results of various types of complications occurring in diabetes (21).

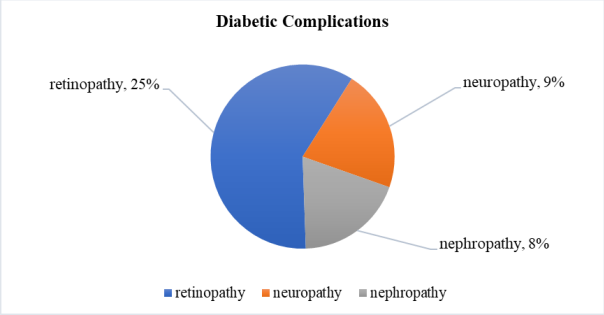

Figure 2: Diabetic complications associated with both mortality and morbidity

13. Diabetic Retinopathy

Among the various complications caused by diabetes, the major one is retinopathy, which affects 12000–24000 patients annually. Retinopathy can result in blindness, however the risk of blindness can decrease by up to 90%, by laser surgery.

14. Neuropathy and Vasculopathy

Lower limb amputation without any trauma is due to neuropathy, which may be caused by DM. In America, 65,700 patients underwent lower limb amputations.

15. End-Stage Renal Disease (Nephropathy)

In the United States, the main contributor to end-stage renal disease is principally type II DM; renal replacement therapy and dialysis were performed on 48,374 and 202,290 patients, respectively, in 2008 (19).

16. Cardiovascular Disease

Individuals with diabetes have 2-4 times more chances to have coronary heart disease than normal people; heart disease is the chief cause of mortality in diabetic patients. Two-thirds of diabetic patients died of a stroke. While women are more prone to suffer from coronary heart disease than men (22).

17. Diagnosis

The criteria for diagnosis of DM as recommended by American Diabetes Association (ADA) is given in Table 3 (23).

18. Glycated Hemoglobin Studies

Glucose in the blood can bind with proteins, so hemoglobin (a protein present in red blood cells) due to its abundance is an easy option for binding; such binding takes place by a non-enzymatic process. As the life span of red blood cells is 120 days, or 3 months, when glycated hemoglobin is measured, it shows the behavior of glucose levels over the previous 2 to 3 months. So, it can be concluded that the measurement of HbA1c can be used to monitor glycemic control for longer periods.

Following is the advantage of the HbA1c test:

- There is no need for fasting and random sampling.
- Shows the history of glucose levels in the blood in the previous 2-3 months.

Table 3: Diagnostic Tests

Sr no.	Test	Range
1	Fasting plasma glucose (FPG)	≥ 126 mg/dL (7.0 mmol/L)
2	Random plasma glucose (RPG)	≥ 200mg/dL (11.1 mmol/L)
3	Oral glucose tolerance test (OGTT)	≥ 200mg/dL (11.1 mmol/L)
4	HbA1c	≥ 6.5%

- The chance of biological variation is less.
- Recently, it has been used as a guide for diabetes management decisions (22).

Due to some limitations in glycated hemoglobin tests, the American Association of Clinical Endocrinologists put HbA1c in the second category of diagnostic tests. 116.

19. Urinary Albumin Studies

All patients with diabetes must underego screening for microalbuminuria on a yearly basis. An amount greater than 30 mg/g indicates albuminuria, which is an indicator of nephropathy.

20. Role of Pharmacist in the Management of DM-11

20.1. Patient Education

Insufficient information regarding self-management of diabetes is being provided to diabetic patients. But contrary to this, an active role must be played by all healthcare providers in patient education. As diabetes is a lifelong syndrome, so will be its education. A study has revealed that individualized patient education has a much better result in controlling poorly controlled diabetes than counselling in group sessions (24).

20.2. Goals

As hyperglycemia is caused by diabetes, which ultimately causes microvascular and macrovascular complications, the goal would be to counter the risk of such complications. In this way, the risk of microvascular and neurologic complications can be controlled by hyperglycemic control. While the risk of macrovascular complications can be prevented by glycemic and hypertension control,

The American Diabetes Association and the European Association for the Study of Diabetes have recommended the following 7 points for the decision of treatment for diabetes (25-27):

1. Every patient must be treated with therapies that fulfil his individualized needs.
2. The foundation of the treatment program would be based on diet, exercise, and patient education.
3. Unless otherwise contraindicated, metformin would be considered the first-line drug in the treatment of type II DM.
4. In the case of uncontrolled diabetes, metformin and one or two oral or injectable drugs have to be added.
5. Finally, when hyperglycemia is still not under control then insulin therapy alone or with other agents has to be initiated.
6. In all kinds of management decisions, the patient's preference must be taken into consideration.
7. Finally, a major focus should be on minimizing of cardiovascular risks.

20.3. Diabetes Medications

20.3.1. Nonpharmacologic Aspects of Diabetes Therapy

American diabetes association (ADA) recommends that diabetic patients be educated about the benefits they get from adequate food, exercise and medication for lowering hyperglycemia. In type II DM, the focus is placed on the consumption of diets that reduce weight. And it must also have the ability to reduce blood pressure and diminish the risk of atherosclerosis. Bariatric surgery cannot only prevent but also reverse type II DM. Rubino et al., 2016 stated that such surgery has a better effect on controlling type II DM than pharmacotherapy (28).

20.3.2. Pharmacotherapy

As type II DM is caused by the combination of insulin resistance by the cells and decreased insulin secretion from beta cells of the pancreas, the management would be either by decreasing the insulin resistance or by enhancing the insulin secretion; a combination of both approaches can be used depending upon the condition of the patient (29).

20.3.3. Sulfonylureas (SU)

This class is also called ATP-sensitive potassium channel blockers. Recently used drugs in this category are tolbutamide, glibenclamide, glipizide, gliclazide, and glimepiride. The following table shows commonly prescribed medications in Pakistan:

Table 4: Sulfonylureas are drugs used in the management management of Diabetic Patients.

Generic Name	Brand Name	Dosage Forms	Kinetics	Dosage Range
Glimepiride	Amaryl, Getryl	Tab 1, 2, 3, 4 mg	P = 2-3 h D = 24 h	I: 1-2 mg/day Mx: 8 mg/day
Glipizide	Glucotrol	Tab 5, 10 mg	P = 1.5-2 h D = 12-24 h	I : 5 mg/day Mx: 40 mg/day

20.3.3.1. Mechanism of action

For the exertion of pharmacological action, this class of antidiabetic medications requires a minimum of 30% working pancreatic beta cells. There are two phases of insulin release, and this class exerts its action by supplementing the second phase, though it has little effect on the first stage. So, in this way, insulin release is increased. Other ancillary effects comprise an enhancement of insulin sensitivity for its receptors, which would lead to a reduction of gluconeogenesis, as well as decreased glucagon release. The mechanism is depicted in the following image:

20.3.3.2. Interactions

A. SU action-enhancer drugs

a) Drugs that displace SU from protein binding: salicylates, sulphonamides, sulfinpyrazone,
b) Drugs that inhibit elimination (metabolism/excretion): these drugs also have synergistic effects. Warfarin, chloramphenicol, sulfonamides, chronic alcohol consumption, and cimetidine
c) Synergistics: salicylates, lithium, theophylline, non-selective beta-blockers like propranolol.

B. SU action diminishers

a) Metabolism inducers: barbiturates, phenytoin, chronic use of alcohol, etc.
b) Drugs that suppress insulin release: thiazides, loop diuretics, oral contraceptives, and corticosteroids (30)

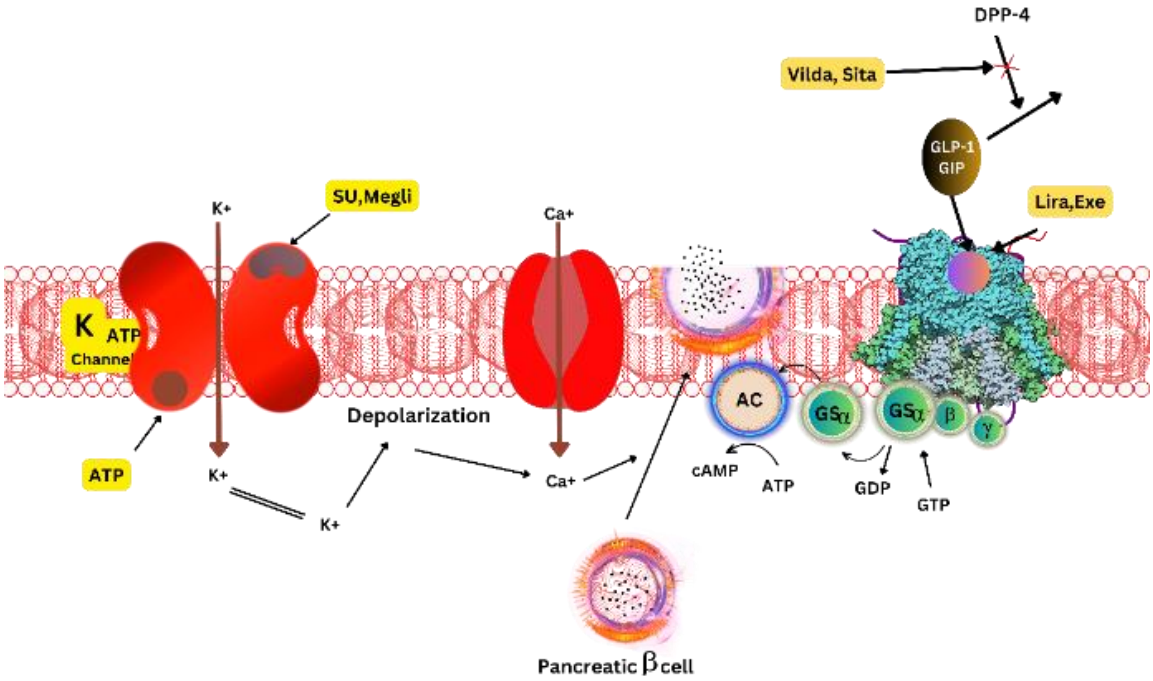

Figure 3: Mechanism of action of Sulfonylureas and Alpha-Glucosidase inhibitors

20.3.3.3. Contraindications

This class is contraindicated under the following conditions:

- Pregnancies because it crosses the placental barrier.
- Lactation because it is released in breast milk.
- Hepatic insufficiency because it is metabolized in the liver, in hepatic insufficiency the level would increase, as would the chances of hypoglycemia as well.
- Renal insufficiency (30, 31).

20.3.3.4. Side Effects

- Increase hypoglycemia because of the strong augmentation of phase II of insulin release.
- Weight gain occurs because more insulin is released, which ultimately performs its anabolic function.
- Rash, photosensitivity, and dizziness (30).

20.3.4. Alpha-Glucosidase Inhibitors

These drugs inhibit alpha glucosidase in the brush border of the small intestine. This enzyme is responsible for the absorption of various sugar-related moieties like disaccharides, dextrin and starch (32). In addition, it also increases the release of an incretin named glucagon-like peptide-1, which contributes to the hypoglycemic effect of the drugs in this class (30). The drugs in this class are acarbose, miglitol, and voglibose.

Table 5: Alpha Glucosidase Inhibitors

Generic Name	Brand Name	Dosage Forms	Dosing Time	Dosage Range
Acarbose	Glucobay	50, 100 mg	Meal-time dosing	I: 25 mg TDS Mx: 100 mg TDS
Miglitol	Glyset	Tab 25, 50, 100 Mg	Meal-time dosing	I: 25 mg TDS M: 100 mg TDS
voglibose	Voglitor	Tab 200, 300mg	Meal-time dosing	200-300S

20.3.4.1. Drug Interactions

- Produce hypoglycemia when added concomitantly used with insulin or other insulin-releasing agents.
- As it decreases the absorption of various kinds of glucose-like substances, it would decrease the absorption of digoxin.

20.3.5. Biguanides

Only one biguanide, named Metformin, is currently in use. Metformin is the first-line drug for type II DM.

20.3.5.1. Mechanism of action

The presence of insulin is necessary for the action of metformin, though it does not cause the release of insulin. So, if a person has type I diabetes or his pancreas is removed, metformin would be ineffective in these conditions.

The mechanism is still ambiguous. But recent studies have shown that an enzyme named protein kinase, whose activation depends on Adenosine Monophosphate, also called AMPK, plays a role in the functioning of metformin.

The following are the key features of its action:

i. The main function is the suppression of gluconeogenesis in the liver, which is the main function by which it lowers the blood glucose level in diabetic patients.
ii. Increases insulin-mediated uptake of glucose by muscle cells and fat cells. In this way, it decreases insulin resistance because, on the one hand, it causes glycogen storage in muscles, while on the other hand, in adipose tissues, it reduces lipolysis and increases fatty acid oxidation.
iii. As depicted in the above picture, metformin mingles with the respiratory chain in mitochondria, which would lead to the utilization of glucose in the periphery by anaerobic glycolysis. This action also yields lactate.
iv. Metformin decreases the absorption of glucose, amino acids, and cyanocobalamin, or vitamin B12, from the intestine.

20.3.5.2. Biguanides Uses

Unless otherwise contraindicated, it is the first-choice drug for diabetes mellitus. It may be used for weight reduction and does not cause hypoglycemia. It has the ability to avert not only microvascular but also macrovascular complications of diabetes. It comes in combination with other oral and injectable antidiabetic drugs. It is also given in combination with insulin to enhance insulin sensitivity.

Table 6: Biguanides

Generic Name	Brand Name	Dosage Forms	Kinetics	Dosage Range
Metformin	Glucophage	Tab 500, 850, 1000 mg	P = 3 h D = 8-12 h	I: 250-500 mg/s Mx: 2500 mg/s

20.3.6. Thiazolidinedione

Table 7: Thiazolidinedione

Generic Name	Brand Name	Dosage Forms	Kinetics	Dosage Range
Pioglitazone	Actos	15, 30, 45 mg	Onset several weeks	I: 15-30mg QD Mx: 45 mg QD

20.3.6.1. Mechanism of action

- Their major site of action is fatty tissue.
- In fatty tissue, it activates the nuclear proliferator-activated receptor γ or PPAR γ which, upon activation, increases the expression of many genes and gives a response to insulin.
- The activation also enhances the expression and translocation of glucose transporter type 4 (GLUT).
- Because of the enhancement of GLUT-4 in the liver, it becomes a cause of suppression of hepatic gluconeogenesis.
- It also activates genes that regulate, in adipose tissues, the metabolism of fatty acids as well as lipogenesis. Overall, this act would lead to the enhancement of insulin sensitivity (30).

20.3.7. Insulin

Banting and Best discovered insulin in 1921 from a pancreas whose exocrine part was removed; they demonstrated that the substance they had discovered had the potential to lower blood glucose levels. In 1926, insulin was crystallized for the first time to obtain its pure form, which was followed by the full demonstration of its chemical structure by Sanger in 1956.

Insulin is synthesized in the beta cells of the pancreas. The very first peptide chain obtained after translation is called Preproinsulin, which has a total of 110 amino acids. Preproinsulin has a molecular weight of 11000. From Preproinsulin 24 amino acids are removed. Now the remaining product is called proinsulin, which has a connecting peptide of 35 amino acids as well as disulfide bonds.

The connecting peptide of the 'C' chain has two specific regions at which the convertase enzyme acts, which are present in the Golgi apparatus. After splicing off the resultant product, insulin and C peptide are stored in granules inside the cell. Insulin is comprised of two chains: chain A, which has 21 amino acids, and chain B, which has 30 amino acids. Both chains are connected by two disulfide bonds, while another disulfide bond is also present in chain A. The molecular weight of insulin is about 6000 (30, 31).

20.3.7.1. Regulation of Insulin Secretion

The human pancreas secretes approximately 1 unit of insulin per hour. But a larger amount of insulin is released after eating a meal. There are various mechanisms, like neural, chemical, and hormonal ones, that regulate the release of insulin from the beta cells of the pancreas.

20.3.7.2. Chemical Mechanism of Release

The beta cells of the pancreas can sense the presence of glucose. Beta cells have glucose transporter 1, or GLUT1, through which glucose can enter; this entry is insulin-independent. After entry, the glucose becomes phosphorylated by glucokinase. Following this metabolism, the ATP-sensitive K+ channels become inactivated. This would result in depolarization, which is followed by the opening of potentially sensitive Ca+2 channels and the release of intracellular Ca2+ from the smooth endoplasmic reticulum. The buildup of Ca+2 in the cell will cause the release of insulin.

The release of insulin from beta cells takes place in two phases: the first phase is very brief and takes place within two minutes, which is then followed by the second phase, which is more delayed but also sustained.

20.3.7.3. Mechanism of Action

Receptor tyrosine kinase, or RTK, is the receptor on which insulin acts. Though such receptors are present in nearly all cells, the fat, liver, and muscle cells have a greater number of such receptors; about 300,000 RTK per cell of the moieties are present. RTK is a heterotetrameric glycoprotein; it has four subunits, of which two are present outside the cell and are called alpha subunits, while the other two are transmembranous and are called beta subunits. Alpha and beta subunits are connected to each other by a disulfide bond. Both units are unique in their functioning because the alpha subunit has a binding site for insulin while the beta subunits have tyrosine kinase activity, as shown in figure 4.

When insulin binds with its receptor, first the receptor undergoes aggregation, and then the whole receptor

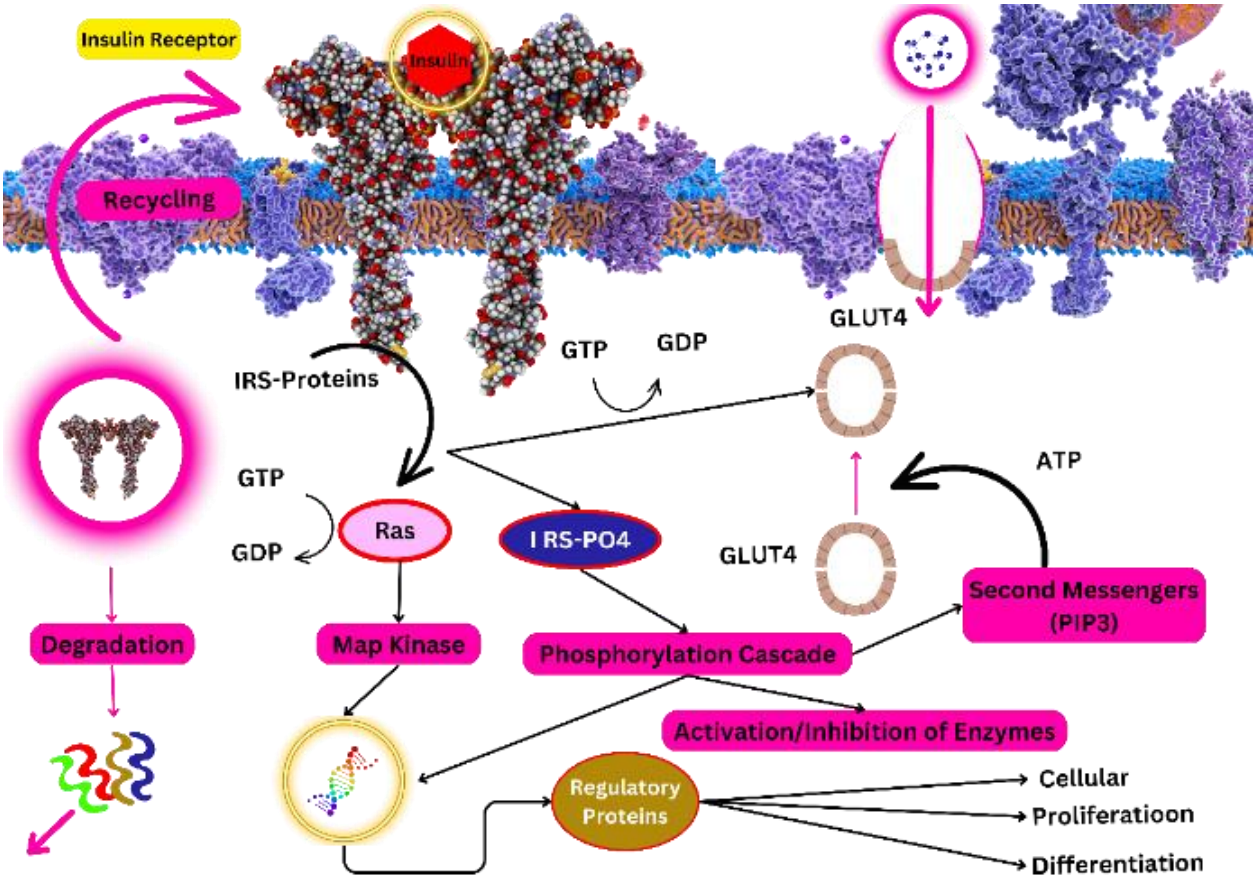

Figure 4: Mechanism of action of insulin

Table 8: Actions of insulin

Actions of insulin to produce hypoglycemia		
Adipose tissue	**Liver**	**Muscle**
Glucose uptake and storage as fat and glycogen	Glucose uptake increased.	Enhanced glucose uptake and usage
Inhibit lipolysis	Glycogen synthesis	Inhibition of proteolysis, as well as the release of pyruvate, lactate, and amino acids into the bloodstream. make the substrates for hepatic gluconeogenesis
Release free fatty acids.	Inhibition of glycogenolysis and glucose production	
Production of substrates for gluconeogenesis	Inhibit gluconeogenesis from precursors like protein, FFA, glycerol, and pyruvate.	

along with the bound insulin molecule is internalized. As soon as internalization happens, this gives the signal for activation of the tyrosine kinase activity of the beta subunits. After activation, both beta subunits phosphorylate one another's tyrosine amino acid. The phosphorylated beta subunits then exposed their catalytic sites to insulin receptor substrate proteins, which are IRS1, IRS2, etc., to phosphorylate their tyrosine residue. This would trigger a torrent of phosphorylation and dephosphorylation reactions. Finally, the signal is amplified, which either stimulates or inhibits the enzymes that are responsible for the metabolic activities of insulin.

20.3.7.4. Actions of Insulin

The actions of insulin are summarized in table 8.

20.3.7.5. Types of Insulin

They are classified into different classes based on onset and time duration: rapid-acting, short-acting, intermediate-acting, long-acting, and pre-mixed (33); some of them are mentioned in tables 9 and 10.

Table 9: Rapid-acting insulin

Type of Insulin/ Brand Names	Onset	Peak	Duration
Humalog or Lispro	15-30 min	30-90 min	3-5 hours
NovoLog or Aspart	10-20 min	40-50 min	3-5 hours
Apidra or Glulisine	20-30 min	30-90 min	1-21/2 hours

Table 10: Short-acting insulin

Type of Insulin/ Brand Names	Onset	Peak	Duration
Regular (R) Humulin or Novolin	30 min-1 hours	2-5 hours	5-8 hours
Velosulin (for use in the insulin pump)	30 min-1 hours	2-3 hours	2-3 hours

20.3.7.6. Insulin Delivery

Most of the time, insulin is injected subcutaneously, while in some conditions like diabetic ketoacidosis, in the ICU, preoperatively, and in labor rooms, insulin is injected intravenously. The most popular form is pens, which are prefilled. Jet injectors provide insulin without pain. The use of long-acting insulin IV, IM, or in an infusion device is not recommended (30).

20.3.7.7. Commonly Used Insulin Regimens

For the provision of the basal level of insulin, long-acting insulins, like glargine, detemir, or degludec are used, and for each meal, premeal short-acting insulins, like lispro, glulisine, regular or aspart can be used. The most common and feasible regimen is the use of intermediate-acting insulin, like NPH is used in combination with regular insulin. So, NPH provides the basal level of insulin while regular insulin is used for mealtime coverage.

The mode of release of insulin from a pump device is shown. 'B', 'L', 'S', and 'HS' are for breakfast, lunch, supper, and bedtime, respectively. The pump releases short-acting insulin-like glulisine at predetermined release rates; it is also set to provide a constant basal rate of insulin (34).

21. Conclusion and Future Perspective

Diabetes Mellitus is a condition characterized by decreased insulin synthesis, increased Glucagon secretion, and the development of insulin resistance in body cells. It may affect individuals younger than 40 years of age and requires long-term medical care. It is influenced by genetic, behavioral, and environmental variables. Depression is also a risk factor. Insulin resistance develops in response to physical inactivity, steroid use, and a high-calorie diet. The early development of beta-cell dysfunction enables beta-cell treatment prior to the onset of diabetes mellitus, which increases morbidity and mortality. Laser surgery can minimize the chance of blindness by up to 90%. The American Diabetes Association (ADA) has established diabetes diagnosis criteria, such as fasting plasma glucose (FPG), random plasma glucose (RPG), oral glucose tolerance test (OGTT), glycated hemoglobin studies, and urine albumin studies. The HbA1c test is used to evaluate long-term glycemic control, and individualized patient education is more helpful than group sessions for sustaining poorly controlled diabetes. Bariatric surgery is superior to medicine, and anti-diabetic medications can either reduce insulin resistance or increase insulin production.

Conflict of Interest The authors declared that they have no competing or conflict of interest.

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