WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on proliferating Diabetes Mellitus disease – A systematic Review

Sanika J Veer *, Miss Priya S Shinde, Shruti More, Dipak jaybhaye, Yash pisal

Yashoada Technical Campus, Satara
Affiliated with Dr. Babasaheb Ambedkar Technology University Lonere, Raigad
Sanuveer28@gmail.com, sanuveer28@gmail.com, priyashinde_pharm@yes.edu.in, Shrutimore908@gmail.com, yashpisal11603@gmail.com
dipakjaybhaye22@gmail.com

Abstract:

The prevalence of diabetes mellitus, the ninth leading cause of death, has quadrupled in the last three decades. Approximately 1 in 11 people worldwide currently have diabetes, with 90% of those with DM. Asia is a major hotspot for the global DM epidemic, with China and India acting as the top two epicentres. While genetic predisposition plays a part in an individual's susceptibility to DM, poor diet and a sedentary lifestyle are major contributors to the current global epidemic; early developmental factors, such as prenatal exposures, also influence a person's later susceptibility to DM.

Making healthy lifestyle choices, such as maintaining a healthy body weight and eating a balanced diet, can help prevent many occurrences of diabetes mellitus. a nutritious diet, regular exercise, and moderate alcohol use. This paper's goal is to evaluate the literature on type 1 and type 2 diabetes, focussing on the disease's pathogenesis and treatment. This study updates the global epidemiology of diabetes mellitus (DM), along with dietary, lifestyle, and other risk factors for DM and its effects.

Key words: Diabetes Mellitus, Types, Pathophysiology, Signs and Symptoms, Diagnosis, Treatment, Pharmaceutical Agents, Insulin therapy.

Introduction:

Diabetes mellitus is a long-term condition affecting how proteins, lipids, and carbs are metabolised. Diabetes mellitus is characterised by a defective or insufficient insulin secretary response, which results in poor utilisation of carbohydrates (glucose), as well as the hyperglycaemias that follow. [1] The most prevalent endocrine condition, diabetes mellitus (DM), is sometimes referred to as a "sugar" and is typically caused by an insufficiency or lack of insulin, or infrequently, by an impairment of insulin function (insulin resistance) [2].According to the International Diabetes Federation (IDF), there are around 40.9 million diabetic subjects in India overall, and by 2025, that number is expected to increase to 69.9 million [3].

Langerhan's. By promoting glycogenesis and transferring glucose to the muscles, liver, and adipose tissue, insulin lowers blood glucose levels. Alpha (α) cells play a crucial role in blood glucose regulation by generating glucagon, which raises blood glucose levels by speeding up glycogenolysis, while neural tissue and erythrocytes do not require insulin for glucose utilisation [4, 5].

Type II diabetes mellitus accounts for 80% to 90% of all occurrences of diabetes mellitus, and it is associated with an increased risk of obesity, metabolic and cardiovascular problems, and cancer in the fetus's postpartum life.[6]

Classification of Diabetes Mellitus:

Insulin dependent type 1 Diabetes Mellitus:

Previously known as juvenile-onset or ketosis-prone diabetes, this form of diabetes mellitus is also referred to as autoimmune diabetes. The person may also seek treatment for further autoimmune conditions such Addison's disease, Hashimoto's thyroiditis, and Graves' disease.[7]

Insulin-dependent diabetes mellitus (IDDM), another name for type I diabetes mellitus, primarily affects children and young people. It typically develops suddenly and can be fatal.[8] .Anti-glutamic acid decarboxylase, islet cell, or insulin antibodies are typically present in type 1 diabetes, indicating the autoimmune mechanisms that result in beta-cell death. According to the American Diabetes Association (2014), type 1 diabetes is caused by b-cell loss, which typically results in complete insulin insufficiency. The rate at which beta-cells are destroyed varies greatly; in some people, it happens quickly, while in others, it happens slowly.[9]

Insulin production is severely reduced or absent as a result of the pancreatic ß-islets cells being destroyed. Insulin injections are necessary for treatment.[10]

Insulin Non dependent type 2 Diabetes Mellitus:

Another name for type 2 diabetes mellitus is adult-onset diabetes. In the context of insulin resistance, the progressive insulin secretary malfunction (American Diabetes Association, 2014)[11] Individuals with this kind of diabetes usually exhibit resistance to insulin's effects. [12] Both forms of diabetes have long-term problems with the kidneys, blood vessels, eyes, and nerves, which are the main reasons for morbidity and mortality.[13] According to Ross and Wilson (2010), the causes are multifaceted, and predisposing factors include obesity, a sedentary lifestyle, ageing (affecting middle-aged and older individuals), and genetics. Patients with these conditions are more likely to experience both macrovascular and microvascular problems.[14,15]

Gestational Diabetes:

Hyperglycemia during pregnancy raises the chance of negative consequences for the mother, foetus, and infant. [16] This risk exists regardless of whether the hyperglycemia takes on the T2D form identified prior to or during pregnancy. Children born to mothers who have gestational diabetes are more likely to grow up to have diabetes.[17] The higher prevalence of pregnancy-related issues, including macrosomia (birth weight greater than 4.5 kg), large-for-gestational-age births, and premature birth, the main cause of preeclampsia and caesarean delivery is hyperglycemia throughout pregnancy, which results in bigger newborns. A number of risk factors, including obesity, advanced maternal age, polycystic ovarian syndrome, a sedentary lifestyle, exposure to environmental contaminants, and a family history of the condition, can affect gestational diabetes.[18]

As previously stated, some criteria are used to identify gestational diabetes, including assessing blood sugar levels during fasting, following a 75 g oral glucose load, and other pertinent factors.[19]

Pathophysiology of Diabetes Mellitus:

Insulin insensitivity brought on by insulin resistance, decreased insulin synthesis, and ultimately pancreatic beta-cell loss are the hallmarks of type 2 diabetes. As a result, there is less glucose transported into the muscle, fat, and liver cells. Hyperglycemia causes an increase in the breakdown of fat.[20,21] When type 1 diabetes initially manifests, patients are typically young (children or teenagers) and not obese. With a 10-fold higher frequency in first-degree relatives of an index case and substantial correlations with specific histocompatibility antigens (HLA types), there is a genetic tendency. Genetically predisposed people must also be exposed to an environmental trigger, like a viral infection, according to studies conducted on identical twins. Pancreatic B cells may be harmed by viral infections, which can also reveal antigens that start an inflammatory reaction that keeps getting worse. Only when over 90% of the B cells have been killed does the patient become clearly diabetic. Insulin deficiency in this type of diabetes attenuates long-term potentiating and may result in learning and memory deficits. Type 2 diabetes is associated with both insulin resistance and impaired insulin secretion, both of which are important in its pathogenesis. Patients with this type of diabetes are typically obese and typically present in adulthood; the incidence increases over time as B-cell function declines. Insulin resistance causes both tau hyperphosphorylation and Aβ plaque formation; during hyperinsulinemia, insulin and Aβ compete for the insulin-degrading enzyme, causing Aβ accumulation and plaque formation; a decrease in insulin receptor signalling inhibits Akt and dephosphorylates (activates) GSK-3β, resulting in tau hyperphosphorylation1.[22,23]

Some common Signs and Symptoms:

When cells in diabetes mellitus are unable to metabolise glucose normally, they essentially starve.[24] Diabetes mellitus's long-term effects include the progressive development of certain complications such as retinopathy, which can result in blindness, nephropathy, which can cause renal failure, and neuropathy, which increases the risk of foot ulcers, Charcot joints, autonomic dysfunctions, and sexual dysfunction.[25]

i)Diabetes raises a person's risk of developing other illnesses. Other symptoms include Gluconeogenesis from body protein and amino acids, which results in tissue breakdown and muscular atrophy and raises blood glucose levels even more.[26]

ii) excessive ketone body production and the breakdown of body fat, which releases part of its energy.[27]

Causes of Diabetes Mellitus:

Disturbances or anomaly in gluco-receptor of ß cell so that they respond to greater glucose concentration or relative ß cell deficiency. In either situation, insulin secretion is hindered; may progress to ß cell failure[28]

i)Peripheral tissues' decreased sensitivity to insulin is caused by "down regulation" of insulin receptors and a decrease in their quantity. There are many hypersensitive and hyperinsulinemic people with normal glycaemic levels who also have dyslipidaemia, hyperuriemia, and abdominal obesity. Relative insulin resistance exists as a result, especially in the liver, muscles, and fat. Hyperinsulinemia has been linked to angiogenesis.[29]

ii) Obesity and excess levels of the hormones glucagon and hyperglycemia lead to a relative lack of insulin, which leads the ß cells to lag behind. According to two views, there are anomalies in nitric oxide metabolism that cause nerve injury and changed perineural blood flow.[30]

Diagnosis of Diabetes Mellitus:

Haemoglobin (HbA1c) plasma glucose levels, the oral glucose tolerance test (OGTT), or fasting plasma glucose (FPG) are frequently used to diagnose diabetes mellitus. In order to establish cut-off values for glucose and HbA1c to diagnose diabetes, these numbers are utilised to estimate the connection between HbA1c or FPG and retinopathy.[31]

Blood sugar, urine sugar, glucose tolerance test, renal threshold of glucose, reduced or increased glucose tolerance, renal glycosuria, extended glucose tolerance curve, cortisone-stressed glucose tolerance test, intravenous glucose tolerance test, and oral glucose tolerance test are all used to diagnose diabetes mellitus.[32]

Despite the fact that approximately 25% of individuals with type 2 diabetes already have microvascular problems at diagnosis, this suggests that the patient has had the condition for more than five years.[33]

It is still predicated on the World Health Organization's (WHO) National Diabetic Group Criteria of 2006 or the American Diabetic Association's (ADA) 1997 guidelines, which call for a single elevated glucose reading accompanied by symptoms (weight loss, polyuria, polydipsia, and polyphagia) or two elevated values of either fasting plasma glucose (FPG) ≥7.0 mmol/L (126 mg/dL) or an oral glucose tolerance test (OGTT) with a plasma glucose level of ≥11.1 mmol/L (200 mg/dL) two hours after the oral dose.[34]

Treatment of Diabetes Mellitus:

In addition to having TOD brought on by MDS, patients with T2D frequently have a number of comorbidities, including dyslipidaemia, preobesity/obesity, CKD, and cardiovascular disease (CVD). Because these conditions are risk factors for CVD and CKD, T2D treatment typically involves the holistic management of MDS, including MASLD, hyperglycemia, dyslipidaemia, hypertension, and preobesity/obesity, by lifestyle modification and required medication to lower TOD, enhance cardiovascular and renal outcomes, prolong life expectancy, and enhance one's standard of living. Notably, diabetic patients do not receive the support they need and may experience detrimental psychological and social effects as a result of the stigma associated with diabetes in the media and society, which includes, for instance, attributing diabetes to an individual's unhealthy diet while neglecting genetic, regional, economic, and social factors. Thus, a growing number of voices have urged society to lessen the stigma associated with diabetes and for individuals to increase their knowledge of the disease in order to prevent self-shame.[35]

The requirement to choose the best hypoglycemic regimen for patients has grown in importance. Personalised treatment that takes into account target organ protection, comorbidities, treatment goals, costs, drug accessibility, and patient preferences can be given based on the acceptable stratification of treatment regimens based on glycaemic targets and current blood glucose levels.[36]

Pharmacological Agents:

Biguanides:

The first-line treatment for lowering blood sugar in type 2 diabetes has been the biguanide drug metformin. This medicine has FDA approval. This drug modifies the liver's sensitivity to insulin, which enhances glycaemic control. However, there is a dearth of information—mostly from case reports—about the negative consequences of metformin. Atypical dreams and, in rare cases, lactic acidosis are two ways that metformin may impair a patient's ability to have a good night's sleep[37]

Sulfonyl Ureas:

Second-line drugs called sulfonylureas are commonly used to treat T2DM in people who are not very fat. Since the introduction of tolbutamide in the 1950s, sulfonylureas have been used to treat type 2 diabetes. Acetohexamide, tolbutamide, chlorpropamide, and tolazamide are classified as first-generation medications, whereas glibenclamide, ligmepiride, gliclazide, glipizide, and gliquidone agents are classified as second-generation agents. The essential agents in the second generation differ from those in the first in that they possess far greater power. Insulin secretagogues called sulfonylureas increase the amount of insulin generated by pancreatic b-cells, lowering plasma glucose levels[38-40]

The main acute side effect of sulfonylureas is an increased risk of hypoglycemia, especially in older patients with hepatic dysfunction, decreased renal function, inadequate oral intake, calorie restriction, alcohol misuse, and other conditions.[41-44]

Meglitinide :

The insulin secretagogues repaglinide and nateglinide, also referred to as "glinides," can help people with type 2 diabetes better control their blood sugar levels when combined with a nutritious diet and regular exercise. Along with diet and exercise, meglitinide derivatives, either alone or in combination with metformin, can assist persons with type 2 diabetes improve their glycaemic control.[45,46]

Cell membrane potential, which is dictated by the inverse relationship between extracellular glucose levels and potassium channels that are sensitive to adenosine triphosphate, is involved in the regulation of insulin generation by pancreatic b-cells. Extracellular glucose is transferred into the cell by glucose transporters 2 (GLUT2). As it enters the body, the cell breaks down glucose and uses and stores adenosine triphosphate (ATP) as energy. By blocking ATP-sensitive potassium channels, which depolarise B-cells, and opening calcium channels, which allow calcium to enter, they enhance the release of insulin. Increased calcium levels in cells boost the production of insulin.[47,48]

Alpha glucosidose inhibitors :

The oral AGIs voglibose, miglitol, and acarbose are used to treat diabetes. A-glucosidase inhibitors prevent carbs from being absorbed in the small intestine. They do this by competitively inhibiting the enzymes that convert complex, non-absorbable carbohydrates into simple, absorbable ones. These include the following enzymes: glucoseamylase, sucrase, maltase, and isomaltase. By delaying the absorption of carbs, they diminish postprandial hyperglycemia, or the rise in blood sugar levels after meals, by roughly 3 mmol/l. Acarbose is the medication in this class that is used and studied the most. Though it is more powerful against glucoamylase, acarbose inhibits a-amylase, sucrase, maltase, and dextranase.

However, lactase b-glucosidase is unaffected. These medications have limited bioavailability, a low rate of stomach absorption, and are removed by faeces. On the other hand, miglitol completely bypasses the stomach and travels through the kidneys. Acarbose undergoes intestinal metabolism, but miglitol and volglibose do not. They are consequently beneficial for those with low glucose tolerance in particular.[49,50]

Thiazolidinediones:

Troglitazone, pioglitazone, and rosiglitazone, often referred to as glitazones, are TZDs that function by making insulin more sensitive to type 2 diabetes. TZDs have been widely used since their launch in the late 1990s due to their therapeutic advantages in addressing insulin resistance and preserving glycaemic control. The first medication approved by the FDA for TZDs is troglitazone. But after three years, it was removed off sale because some patients had severe liver toxicity. There are now just two TZDs drugs on the market for clinical use: pioglitazone and rosiglitazone. It is also known that TZDs have anti-inflammatory and anti-cancer properties.[51]

TZDs help patients with type 2 diabetes because they reduce insulinemia, dyslipidaemia, and glycemia. Genes linked to glucose and lipid homeostasis are altered by their activation of the nuclear receptor peroxisome proliferator-activated receptor-g (PPAR-g). Signalling PPAR-g via many mechanisms increases insulin sensitivity. It uses three distinct methods to accomplish this: It 1) raises GLUT4 expression; 2) regulates the release of adipocyte-derived signalling molecules that affect muscle's insulin sensitivity; and 3) triggers death in adipose tissue, resulting in the development of smaller, more flexible adipocytes.[52]

Insulin Therapy:

The primary treatment for all individuals with type 1 diabetes is insulin. Initially, individuals with type 1 diabetes typically require multiple daily injections. Usually, 0–15 minutes of fast-acting insulin or rapid-acting insulin analogue are given along with one or more daily separate injections of intermediate- or long-acting insulin. Every day, two or three readymade insulin shots can be used. All children with type 1 diabetes, especially preschool-aged children, should aim for a HbA1c of less than 7.5% (less than 58 mmol/mol).[53]

The goal of insulin therapy should be to emulate nature, which is incredibly effective in reducing postprandial hyperglycemia and avoiding hypoglycemia in between meals[54]

The location of insulin injection administration, which can be administered intramuscularly or intravenously, is equally crucial for the improved and secure action of insulin. Human, cow, and pork insulin are among the various forms of insulin that are accessible. Adverse effects and complications are not exclusive to insulin therapy. When an incorrect insulin dosage is administered and meals and insulin injections are not coordinated, the most significant side effects are weight gain and hypoglycemia [55,56]

Weight gain is an inevitable side effect of beginning insulin therapy for uncontrolled diabetes since it results from an increase in muscle mass and truncal fat. This is also a result of less energy being lost through glycosuria[57,58]

Many advancements have been achieved to attain strict glucose control and to make administering insulin easier and more accurate. These include insulin syringes, pen devices, insulin pumps, implanted pumps, inhaled insulin, and other insulin administration methods.[59]

Conclusion:

Diabetes has no known cure and progresses slowly. However, with timely treatment and proper knowledge, its effects can be minimised. Three major outcomes are heart attacks, kidney damage, and blindness. Maintaining close monitoring of patients' blood glucose levels is essential to preventing problems. One of the problems with rigorous blood glucose control is that it may result in hypoglycemia, which can have considerably more detrimental effects than an increase in blood sugar. Currently, researchers are searching for novel approaches to diabetes treatment. This study aims to give a summary of recent studies on diabetes.

Acknowledgment:

The completion of an inter- disciplinary project depends upon cooperation , coordination, and combined efforts of several sources of knowledge . I express my depest sense of gratitude from the bottom of my heart to my respected and beloved guide Prof. Miss. Priya Shinde department of pharmacology YSPM'S College of pharmacy, satara for excellent guidance, critical supervision and keep interest and continuous encouragement throughout the study. Her active guidance helped me to develop skills and insight In research and scientific presentation. I am thankful to her for providing immense guidance , valuable advice and direction ; whenever I approached her with a problem.

Reference:

1) Kumar CR. Basic Pathology, Prism PVT. Limited Bangalore, 5th edition, 1992, 569-587.
2) Ross and Wilson. Anatomy and Pathophysiology in Health and Illness, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229.
3) Bacchetta R, Passerini L, Gambineri E, Dai M, Allan SE. Defective regulatory and effector T cell functions in patients with FOXP3 mutations, J Clin Invest. 2006; 116:1713-1722,
4) Wassmuth R, Lernmark A. The genetics of susceptibility to diabetes, ClinImmunol, Immunopathol. 1989; 53:358- 399,
5) 5. Atkinson MA, Eisenbarth GS. Type 1 diabetes new perspectives on disease pathogenesis and treatment, Lancet. 2001; 358:221-229.
6) Hoet JJ, Tripathy BB, Rao RH, Yajnik CS. Malnutrition and diabetes in the tropics, Diabetes Care. 1996; 19:1014-17,
7) Jun SK, Yoon YW. A new look at viruses in Type 1 diabetes, Diabetes/Metabolism Research and Reviews. 2002; 19:8-31.
8) Wassmuth R, Lernmark A. The genetics of susceptibility to diabetes, ClinImmunol, Immunopathol. 1989; 53:358-399,
9) Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight,maternal obesity, and gestational diabetes mellitus Pediatrics, 2005, 115.
10) Wassmuth R, Lernmark A. The genetics of susceptibility to diabetes, ClinImmunol, Immunopathol. 1989; 53:358- 399,
11) Leonardo Jacob S, Pharmacology. The national medical series from Williams and Wilkins Bartiarco, Hong Kong, London, 3rd edition, 1987, 221-225.
12) Blood A, Hayes TM, Gamble DR. Register of newly diagnosed diabetic children, BMJ. 1975; 3:580-583.
13) Kumar CR. Basic Pathology, Prism PVT. Limited Bangalore, 5th edition, 1992, 569-587
14) Tripathi KD. Essentials Medicals Pharmacology, Jaypee Brothers Medical Publisher (P) LTD, 7th edition, 2013, 258-281.
15) . Dyck PJ, Kratz KM, Karnes JL. The prevalence by staged severity of various types of diabetic neuropathy retinopathy and nephropathy in a population-basedcohort: the Rochester Diabetic Neuropathy Study, Neurology, 1993; 43:817-24
16) M.L. Geurtsen, E.E. van Soest, E. Voerman, E.A. Steegers, V.W. Jaddoe, R.J. D. Gaillard, High maternal early-pregnancy blood gluc niose levels are associated with altered fetal growth and increased risk of adverse birth outcomes 62 (10) (2019) 1880–1890, https://doi.org/10.1007/s00125-019-4957-3.
17) M.H. Hollander, K.M. Paarlberg, A.J.J.O. Huisjes, Gestational diabetes: a review of the current literature and guidelines, G. Surv. 62 (2) (2007) 125–136, https://doi. org/10.1097/01.ogx.0000253303.92229.59.
18) J.F. Plows, J.L. Stanley, P.N. Baker, C.M. Reynolds, M.H.J.Ijoms Vickers, The pathophysiology of gestational diabetes mellitus 19 (11) (2018) 3342, https://doi. org/10.3390/ijms19113342.
19) C.F. Chukwunyere, D.O. Awonuga, O.F. Adesina, I.C.J.D. Udenze, Gestational diabetes: Comparison of random and fasting plasma glucose as modalities of screening, 2020. https://www.emjreviews.com/wp-content/uploads/2020/11/ Gestational-Diabetes-Comparison-of-Random-and-Fasting-Plasma-Glucose-as-Modalities-of-Screening.pdf.
20) Kahn, C.R., Banting Lecture. Insulin action, diabetogenes, and the cause of type II diabetes. Diabetes, 43(8): 1066-1084 (1994)
21) 16. Robertson, R.P., Antagonist: diabetes and insulin resistance–philosophy, science, and the multiplier hypothesis. J Lab Clin Med 125(5): 560-564 (1995)
22) Rang, H.P., Dale M.M., Pharmacology, Sixth Edition, Churchill Livingstone. "The Endocrine Pancreas and Control of Blood Glucose, 2008, Page No. 397-409.
23) Sims-Robinson, C., Kim, B., Rosko, A., How does diabetes accelerate Alzheimer disease pathology? Nat Rev Neurol; 6(10): 551-559 (2010)
24) Ross and Wilson. Anatomy and Pathophysiology in Health and Illness, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229.
25) Gupta OP, Joshi MH, Daves SK. Prevalence of Diabetes in India, Adv Metab Disord. 1978; 9:147-65.
26) Kumar CR. Basic Pathology, Prism PVT. Limited Bangalore, 5th edition, 1992, 569-587.
27) Ross and Wilson. Anatomy and Pathophysiology in Health and Illness, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229
28) Alemu S, Dessie A, Seid E. Insulin-requiring diabetes in rural Ethiopia: should we reopen the case for malnutrition- related diabetes, Diabetologia. 2009; 52:1842-1845.
29) Gupta OP, Joshi MH, Daves SK. Prevalence of Diabetes in India, Adv Metab Disord. 1978; 9:147-65.
30) Alemu S, Dessie A, Seid E. Insulin-requiring diabetes in rural Ethiopia: should we reopen the case for malnutrition- related diabetes, Diabetologia. 2009; 52:1842-1845.

31) T. Nakagami, M. Tominaga, R. Nishimura, N. Yoshiike, M. Daimon, T. Oizumi, N.J. Dr Tajima, c practice, globin A1c alone an efficient screening test for undiagnosed diabetes? Jpn. Is. Meas. glycated hemoNational Diabetes Surv. 76 (2) (2007) 251–256, https://doi.org/10.1016/j.diabres.2006.09.015. S. Genuth, K.G.M.M. Alberti, P. Bennett, J. Buse, R. DeFronzo, R. Kahn, J. Kitzmiller, W. C. Knowler, H. Lebovitz, A. Lernmark, D. Nathan, Follow-up report on the diagnosis of diabetes mellitus, Diabetes care 26 (11) (2003) 3160–3167.

32) Mohan V, Pradeepa R. Epidemiology of diabetes in different regions of India. 2009; 22:1-18.

33) Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care 1992 Jul;15(7):815- 819.

34) Cox EM, Elelman D. Test for screening and diagnosis of type 2 diabetes. Clin Diabetes 2009;4(27):132-138

35) Speight, J. et al. Bringing an end to diabetes stigma and discrimination: an international consensus statement on evidence and recommendations. Lancet Diabetes Endocrinol. 12, 61–82 (2024).

36) Zhang, F. et al. Expert consensus on personalized initiation of glucose-lowering therapy in adults with newly diagnosed type 2 diabetes without clinical cardi-ovascular disease or chronic kidney disease. J. Evid. Based Med. 15, 168–179 (2022).

37) Sola D, Rossi L, Schianca GP, Maffioli P, Bigliocca M, Mella R, et al. Sulfonylureas and their use in clinical practice. Arch Med Sci. (2015) 11:840–8. doi: 10.5114/aoms.2015.53304

38) Sola D, Rossi L, Schianca GP, Maffioli P, Bigliocca M, Mella R, et al. Sulfonylureas and their use in clinical practice. Arch Med Sci. (2015) 11:840–8 doi: 10.5114/aoms.2015.53304

39) Khunti K, Chatterjee S, Gerstein HC, Zoungas S, Davies MJ. Do sulphonylureas still have a place in clinical practice? Lancet Diabetes Endocrinol. (2018) 6:8232. doi: 10.1016/s2213-8587(18)30025-1

40) Kalra S, Bahendeka S, Sahay R, Ghosh S, Md F, Orabi A, et al. Consensus recommendations on sulfonylurea and sulfonylurea combinations in the Management of type 2 diabetes mellitus - international task force. Indian J Endocrinol Metab. (2018) 22:132–57. doi: 10.4103/ijem.IJEM_556_17.

41) Sola D, Rossi L, Schianca GP, Maffioli P, Bigliocca M, Mella R, et a Sulfonylureas and their use in clinical practice. Arch Med Sci. (2015) 11:840–8.doi: 10.5114/aoms.2015.53304

42) Khunti K, Chatterjee S, Gerstein HC, Zoungas S, Davies MJ. Do sulphonylureas still have a place in clinical practice? Lancet Diabetes Endocrinol. (2018) 6:821 32.doi: 10.1016/s2213-8587(18)30025-1

43) Kalra S, Bahendeka S, Sahay R, Ghosh S, Md F, Orabi A, et al. Consensus recommendations on sulfonylurea and sulfonylurea combinations in the management of type 2 diabetes mellitus - international task force. Indian J Endocrinol Metab. (2018) 22:132–57. doi: 10.4103/ijem.IJEM_556_17

44) Zaman MSZ, Hassan PH, Islam SMSI, Ullah MAU, Rabbani MGR. Comparative efficacy of insulin, biguanides and sulfonylureas in the glycemic control of newly diagnosed diabetes mellitus patients in Rajshahi, Bangladesh. J Biosci. (2023) 31:39–49.doi: 10.3329/jbs.v31i1.69533

45) Tahrani AA, Barnett AH, Bailey CJ. Pharmacology and therapeutic implications of current drugs for type 2 diabetes mellitus. Nat Rev Endocrinol. (2016) 12:566–92.doi: 10.1038/nrendo.2016.86

46) Keegan MT. Endocrine pharmacology. Pharmacol Physiol anesthesia: Elsevier;. (2019) p:708–31. doi: 10.1016/B978-0-323-48110-6.00036-3

47) Keegan MT. Endocrine pharmacology. Pharmacol Physiol anesthesia: Elsevier;. (2019) p:708–31. doi: 10.1016/B978-0-323-48110-6.00036-3

48) Fridlyand LE, Jacobson DA, Philipson LH. Ion channels and regulation of insulin secretion in human b-cells: a computational systems analysis. Islets. (2013) 5:1–15. doi: 10.4161/isl.24166

49) Derosa G, Maffioli P. [amp]]alpha;-Glucosidase inhibitors and their use inclinical practice. Arch Med Sci. (2012) 8:899–906. doi: 10.5114/aoms.2012.31621

50) Hossain MA, Pervin R. Chapter 34 - current antidiabetic drugs: review of their efficacy and safety. In: Bagchi D, Nair S, editors. Nutritional and Therapeutic Interventions for Diabetes and Metabolic Syndrome, 2nd ed. Amsterdam, The Netherlands: Academic Press (2018). p. 455–73.

51) Damkaci F, Szymaniak AA, Biasini JP, Cotroneo R. Synthesis of thiazolidinedione compound library. Compounds. (2022) 2:182–90. doi: 10.3390/compounds2030013

52) Dubois M, Vantyghem MC, Schoonjans K, Pattou F. Thiazolidinediones in type 2 diabetes. Role of peroxisome proliferator-activated receptor gamma (PPARgamma). Ann Endocrinol (Paris). (2002) 63:511–23.

53) Silver B, Ramaiya K, Andrew SB, Fredrick O, Bajaj S, Kalra S, et al. ADSG guidelines: insulin therapy in diabetes. Diabetes Ther. (2018) 9:449–92. doi: 10.1007/s13300-018-0384-6

54) Ciofeta, M., Lalli, C., Del, S. P. Contribution of postprandial versus interprandial blood glucose to HbA1c in type I diabetes on physiologic intensive therapy with lispro insulin at mealtime. Diabetes Care. 22: 795-800 (1999)

55) Henry, R.R., Gumbiner, B.N., Ditzler, T. Intensiveconventional insulin therapy for type II Diabetes. Metabolic effects during 6-month outpatient trial. Diabetes Care, 16: 21-31 (1993)

56) Kudlacek, S., Schernthaner, G. The effect of insulin treatment on HbA1c, body weight and lipids in type 2 diabetic patients with secondary-failure to sulfonylureas. A five-year follow-up study. HormMetab R., 24: 478-483 (1992)

57) Diabetes Control and Complications Trial Research Group. The effects of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Eng J Med., 329: 977-986 (1993)

58) Yki-Jarvinen, H., Ryysy, L., Nikkilä, K., Tulokas, T.,Vanamo, R,, Heikkila, M. Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus: a randomized trial. Ann Intern Med; 130: 289-396 (1999)

59) Gupta OP, Joshi MH, Daves SK. Prevalence of Diabetes in India, Adv Metab Disord. 1978; 9:147-65