International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

# A Review on Comorbidity of Diabetes Mellitus

**Akanksha Lokhande[1], Nitin Kale[2], Gajanan Sanap[3]**

[1]Student, LBYP
[2]Guide, LBYP
[3]Principal, LBYP

**Abstract**
Diabetes mellitus is a metabolic disorder that result from a relative or absolute deficiency of insulin , which affect carbohydrate, proteins and fat metabolism. Patient with diabetes mellitus may also have other comorbidities and complication, which require treatment. This review paper investigate the major comorbid condition and complication that occurs in patient with diabetes ,their management and their influence on diabetes therapy. Comorbidities and complications occurs in every organ system in the body. Diabetic complication includes nephropathy, neuropathy, retinopathy and cardiovascular disease. Their treatment includes the use of multiple medications.

**KEYWORDS**: diabetes mellitus, comorbidity, complication

**Introduction:**
Diabetes mellitus (DM) is commonest endocrine complaint that affects further than 100 million people worldwide( 6 population). It's caused by insufficiency or ineffective product of insulin by pancreas which results in increase or drop in attention of glucose in the blood. It's set up to damage numerous of body systems particularly blood vessels, eyes, heart and nerves. (dementia depressing, anxiety that is diabetic retinopathy, nephrotoxicity, hepatotoxicity, cardiatoxicity Diabetes mellitus has been classified into two types i.e. insulin dependent diabetes mellitus (IDDM, Type I) and non insulin dependent diabetes mellitus (NIDDM, Type II). Type I diabetes is an autoimmune complaint characterized by an original seditious response in and around islands that's followed by picky destruction of insulin concealing cells whereas Type II diabetes is characterised by supplymental insulin resistance and blood vessels(1).

**Epidemiology and pathophysiology:**
The complaint burden related to diabetes is high and rising in every country, fueled by the global rise in the frequence of rotundity and unhealthy cultures. The rearmost estimates show a frequence rate of 11.1 with diabetes in 2019, anticipated to rise to 13 by 2045 Northern America and Caribbean regions the frequence rate is most pronounced in the middle east and north African regions which are prognosticated to rise 13.9 by 2045. The smallest frequence rate( 4.7) is observed in Africa which is anticipated to increase to 5.2 in 2045 In general, countries in South- East Asia and South America have moreover high or intermediate frequentness According to a recent study by Saeedi et al. in 2019, a global frequence of 463 million people with diabetes was recorded which represents a 9.3 frequence rate worldwide. By 2030 this frequence rate is estimated to reach 10.2 and by 2045 to 10.9. The region-stratified diabetes frequence is calculated for several countries which display the countries with the

loftiest number of diabetic cases in 2019, worldwide the top 10 countries or homes for the number of people with diabetes are linked Among these countries, China has the loftiest proportion of diabetic cases at around 116 million. India seconds the list at 77 million followed by the United States of America at 31 million demonstrating the US as one of the most diabetic threat countries in the forthcoming decade. Pakistan, Brazil, and Mexico are those projected to the high- end diabetic groups with diabetic cases at around 19 million, 16 million, and 12 million, independently. While Bangladesh falls in the lower end of this list, the country's adding population and lack of well- planned intervention strategies make it no lower diabetic threat than the US(2).

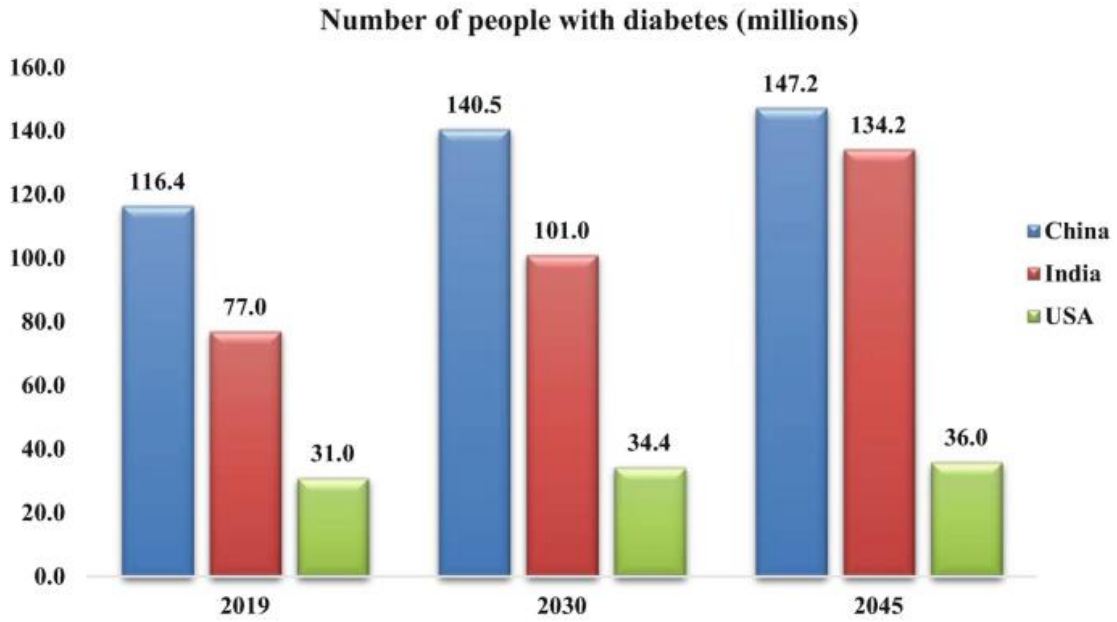



**Fig:1 epidemiology of diabetic: a global view**

**Diabetes in India**

According to recent estimates, approximately 285 million people worldwide (6.6%) in the 20–79 year age group will have diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world". According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are take

**Pathophysiological aspects:**

Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure. This leads to a decrease in glucose transport into the liver, muscle cells and fat cells. There is an increase in the breakdown of fat with hyperglycemia . Type 1 diabetic patients are usually young (children or adolescents) and not obese when they first develop symptoms. There is an inherited predisposition, with a 10-fold increased incidence in first-degree relatives of an index case, and strong associations with particular histocompatibility antigens (HLA types). Studies of identical twins have shown that genetically predisposed individuals must

additionally be exposed to an environmental factor such as viral infection ,Viral infection may damage pancreatic B cells and expose antigens that initiate a self-perpetuating autoimmune process. The patient becomes overtly diabetic only when more than 90% of the B cells have been destroyed. In this type, insulin deficiency attenuates long term potentiating and might lead to deficits in learning and memory. Type 2 diabetes is accompanied both by insulin resistance and by impaired insulin secretion, each of which are important in its pathogenesis. Such patients are often obese and usually present in adult life, the incidence rising progressively with age as B-cell function declines. In this insulin resistance leads to both Aβ plaque formation and tau hyper-phosphorylation. During hyperinsulinemia , insulin and Aβ competes for insulin degrading enzyme, leading to Aβ accumulation and plaque formation. A decrease in insulin receptor signaling leads to inhibition of Akt and dephosphorylation (activation) of GSK-3β and results in tau hyperphosphorylation (2)

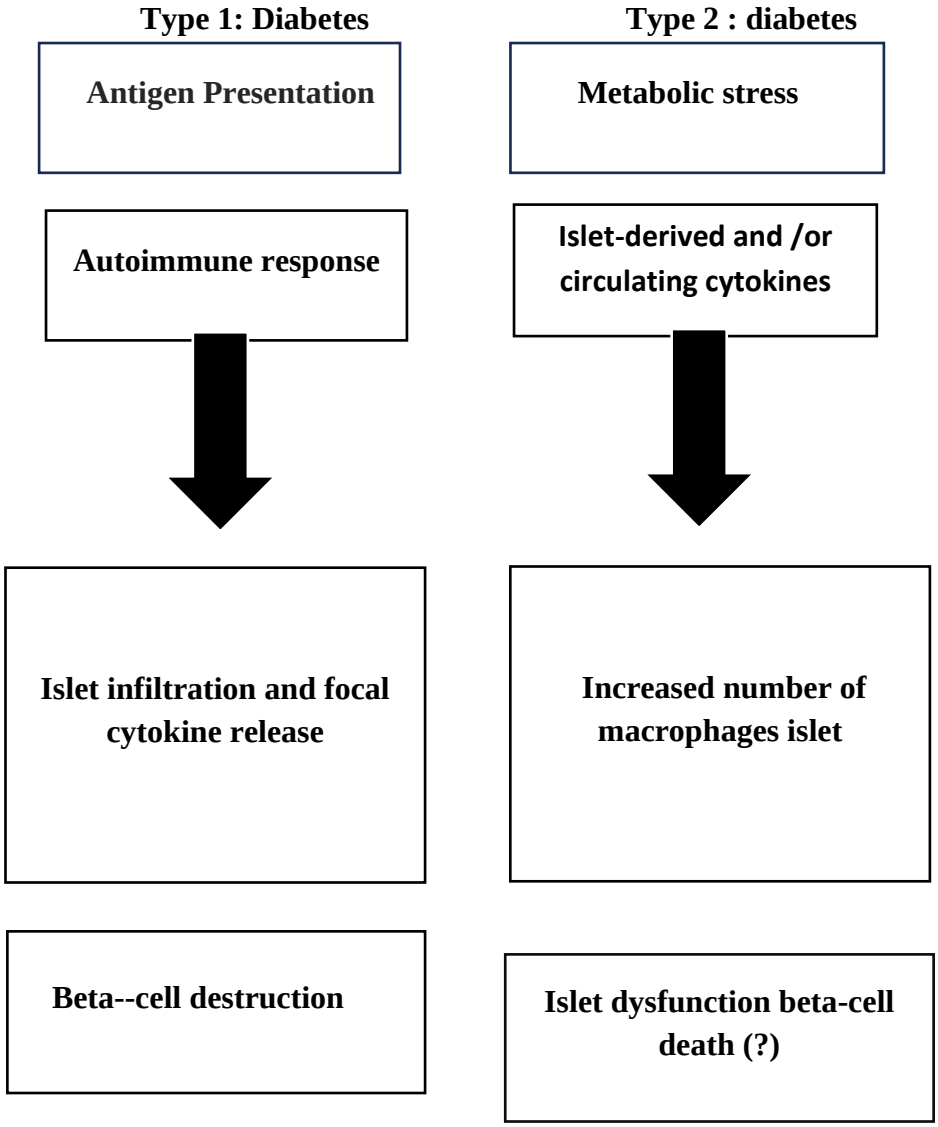



**Fig: 2 pathophysiology of diabetes mellitus**

T2DM is a multifactorial disease involving genetic and environmental factors. The pathophysiological changes are characterized by β-cell dysfunction, insulin resistance and chronic inflammation, all of

which progressively hamper control of blood glucose levels and lead to the development of micro- and macro-vascular complications. With respect to hyper-glycaemia at least eight distinct pathophysiological abnormalities contribute to impaired glucose homeostasis and these factors are already well established early in the natural his- tory of T2DM. To the 'ominous octet' we can add two additional pathophysiological abnormalities: activation of inflammatory pathways and impaired insulin mediated vasodilation, which both contribute to muscle insulin

**Insulin resistance:**

Obesity and physical inactivity lead to insulin resist- ance, which together with a genetic predisposition45, place stress on β-cells, leading to a failure of β-cell function and a progressive decline in insulin secre-tion(3)nsulin resistance precedes T2DM by many years. Insulin resistance is not only present in muscle and the liver, the two tissues responsible for the majority of glucose disposal following carbohydrate

Systemic inflammation is a well-documented contributor to insulin resistance. Increased levels of pro-inflammatory cytokines, such as IL-6 and TNF, and increased numbers of macrophages and other (4)

**Imflammation**:

Systemic inflammation is a well-documented contributor to insulin resistance. Increased levels of pro-inflammatory cytokines, such as IL-6 and TNF, and increased numbers of macrophages and other inflammatory cells are observed in adipose tissue, livers and sera of patients and animals in insulin-resistant states (5)Pro-inflammatory cytokines induce insulin resistance by activating downstream kinases, including IκB kinase-β (IKKβ), JUN amino-terminal kinase 1 (JNK1; also known as MAPK8) and p38 MAPK, which can contribute to the phosphorylation of serine residues in IRS proteins and stimulate production of suppressors of cytokine signaling (SOCS), which block the action of IRS proteins. Blocking TNF activity with antibodies or knockout of its receptor improves insulin sensitivity in obese mice (6) (7) but TNF-specific blocking agents do not improve glycemic control in patients with T2DM.(8) Conversely, pharmacological and genetic inhibition of the IKKβ–nuclear factor-κB (NF-κB) path- way improves insulin sensitivity in mice and improves glycemic control in patients with T2DM albeit modestly.(9)

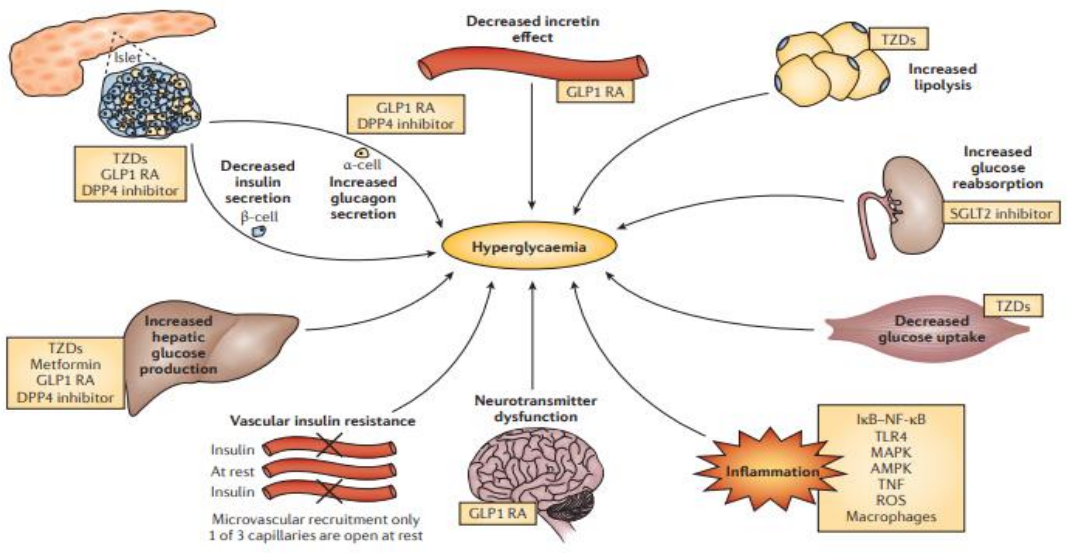


**Figure:3|** The 'ominous octet' of hyperglycaemia in T2DM. Insulin resistance in muscle and the liver, and impaired insulin secretion by the pancreatic β-cells are the core defects in type 2 diabetes mellitus (T2DM). β-cell resistance to glucagon-like peptide 1 (GLP1) contributes to progressive failure in the function of β-cells, whereas increased glucagon levels and enhanced hepatic sensitivity to glucagon contribute to the excessive glucose production by the liver. Insulin resistance in adipocytes results in accelerated lipolysis and increased plasma free fatty acid (FFA) levels, both of which aggravate the insulin resistance in muscle and the liver and contribute to β-cell failure. Increased renal glucose reabsorption by the sodium/glucose co-transporter 2 (SGLT2) and the increased threshold for glucose spillage in the urine contribute to the maintenance of hyperglycaemia. Resistance to the appetite-suppressive effects of insulin, leptin, GLP1, amylin and peptide YY, as well as low brain dopamine and increased brain serotonin levels contribute to weight gain, which exacerbates the underlying resistance. To the 'ominous octet' must be added vascular insulin resistance and inflammation, making the 'decadent decoplet'. AMPK, AMP-activated protein kinase; DPP4, dipeptidyl peptidase 4; IκB, inhibitor of NF-κB; MAPK, mitogen-activated protein kinase; NF-κB, nuclear factor-κB; RA, receptor agonist; ROS, reactive oxygen species; TLR4, Toll-like receptor 4; TNF, tumour necrosis factor; T

**Diagnosis of DM:**

The designation of polygenic disease in associate degree symptomless subject ought to never be created on the idea of one abnormal blood sugar value. If a designation of polygenic disease is formed, the practitioner should feel assured that the designation is totally established since the consequences for the individual area unit extensive and long. The designation of polygenic disease mellitus embrace, excretory product sugar, blood sugar, aldohexose tolerance check, urinary organ threshold of aldohexose, diminished aldohexose tolerance, exaggerated aldohexose tolerance, renal symptom, extended aldohexose tolerance curve, cortisone stressed aldohexose tolerance check, endovenous aldohexose tolerance test, oral aldohexose tolerance check (10)

According to the American Diabetes Association (ADA), the fasting glucose concentration should be used in routine screening for diabetes; but postprandial blood sugar, random blood sugar and glucose tolerance test are also used for blood sugar determination. For the diagnosis of diabetes, at least one criterion must apply:

- Symptoms of diabetes (polyuria , polydipsia, unexplained weight loss, etc) as well as casual plasma glucose concentration = 11.1 mmol /L (200 mg/dL).
- Fasting plasma glucose = Its normal range is 70-110 mg/dl with no caloric intake for at least 8 h.

The World Health Organization (WHO) classification includes both clinical stages normoglycaemi , impaired glucose tolerance/impaired fasting glucose (IGT/IFG), diabetes) and etiological types of diabetes mellitus, identical to the ADA except that WHO group includes classification formerly known as gestational impaired glucose tolerance (GIGT) and GDM: fasting glucose = 7.0 mmol/L (126 mg/dL) and/or 2-h glucose = 7.8 mmol/L (140 mg/dL) after a 75-g OGTT .(11)

**Some comman sign and symptoms:**

In DM, cells fails to metabolized aldo hexose within the normal manner, effectively become starved. The long run effect of DM which incorporates progressive development of the particular complications of retinopathy with potential visual defect, renal disorder which will result in failure ,and pathology with risk of foot ulceration, neurologist joint and features of involuntary pathology and sexual dysfunction

People with polygenic disease area unit at will increase risk of disease (12)Other, varied symptoms area unit determined due to Gluconeogenesis from amino acids and body macromolecule, causing muscle wasting, tissue breakdown and more increases the blood sugar level. ii. destructive metabolism of body fat, cathartic a number of its energy and excess production of organic compound bodies(13)

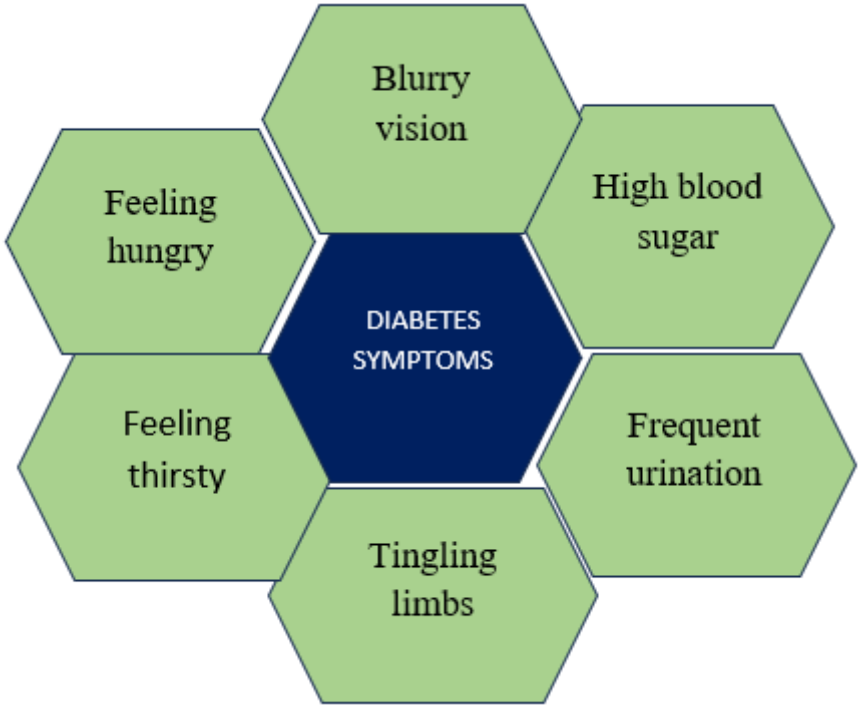



**FIG: 4 symptoms of diabetes**

**Treatment of DM:**

The treatment is to beat the causative cause and to give high doses of normal hypoglycaemic agent. The hypoglycaemic agent demand comes back to traditional once the condition has been controlled the aims of management of DM will be achieved by: 1. to revive the disturbed metabolism of the diabetic as nearly to traditional as is according to comfort and safety. 2. to forestall or delay progression of the short and long run hazards of the unwellness. to supply the patient with data, motivation and means to undertake this own enlightened care. A. styles of medical aid concerned In DM 1 vegetative cell medical aid Researchers have shown that monocytes/ macrophages is also main players that contribute to those chronic inflammations and hypoglycaemic agent resistance in T2DM patients(14)vegetative cell professional medical aid, a completely unique technology, is intended to regulate or reverse immune dysfunctions. The procedure includes: assortment of patients‘ blood current through a control system, purification of lymphocytes from the entire blood, co-culture of them with adherent twine blood-derived multi-potent stem cells (CB-SCs) in vitro and administration of the educated lymphocytes (but not the CB-SCs) to the patient‘s circulation(15)

**Insulin and oral hypoglycemic drugs:**

of calcium ions and subsequent secretion of preformed insulin granules. Acute administration of sulfonylureas to type 2 DM patient’s increases insulin release from the pancreas and also may further increase insulin levels by reducing hepatic clearance of t Insulin therapy should aim to mimic nature,

which is remarkably successful both in limiting postprandial hyperglycemia and preventing hypoglycemia between meals(1)Site of administration of insulin injection is equally important for better and safe action of insulin and can be given by intramuscular or intravenous route. Different preparations of insulin are available such as human insulin, beef insulin, pork insulin. Insulin therapy is no free from complications and adverse effects. The most important adverse effect are weight gain and hypoglycemia when inappropriate dose of insulin is taken and when there is mismatch between meals and insulin injection . Weight gain after starting insulin therapy for uncontrolled diabetes is an inevitable consequence and is the result of increased truncal fat and muscle bulk. This is also due to reduced energy losses through glycosuria Sulphonyl ureas such as glibenclamide, glipizide and biguanides such as metformin, phenformin are oral hypoglycemic drugs(16)Sulfonylureas cause hypoglycemia by stimulating insulin release from pancreatic ß-cells. They bind to sulfonylurea (SUR) receptors on the ß-cell plasma membrane, causing closure of adenosine triphosphate (ATP)- sensitive potassium channels, leading to depolarization of the cell membrane. This in turn opens voltagegated channels, allowing influx he hormone. Initial studies showed that a functional pancreas was necessary for the hypoglycemic actions of sulfonylureas . Biguanides such as metformin is antihyperglycaemic , not hypoglycemic. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doseS(17)It has been shown to increase peripheral uptake of glucose, and to reduce hepatic glucose output by approximately 20-30% when given orally but not intravenously. Impaired absorption of glucose from the gut has also been suggested as a mechanism of ac tion (1).

**Therapeutic overview: present and perspective:**

Appropriate diet, weight reduction and physical activity are the cornerstones of the treatment of type 2 diabetes, but the achievement of optimal glycaemic control, which is essential for the prevention of diabetes related complications, generally requires the use of antidiabetic drugs. None of these are able to correct all the anomalies involved in the pathogenesis of type 2 diabetes. So, they generally fail after a few years of evolution of the disease Combination therapies and even insulin also rarely achieve durable glycaemic control and expose the patient to side effects, particularly hypoglycaemia and weight gain. This explains the intensive pharmacological research of new drugs targeting β-cell function and the response of insulin sensitive tissues, with the aims to reduce therapeutic side effects, to preserve β-cell function and to prevent diabetes related complications (18)

**Sulphonylureas:**

The oldest class of oral antidiabetic agents has dominated the market for many years. Presently, sulfonylureas (SU) are no longer recommended as first linetherapy in the majority of type 2 diabetic patients, but they remain indispensable in the later stages of the disease. The effect of SU on insulin secretion is known since the early experiments of Loubatières , but their mechanism of action at the cellular level has only been discovered 12 years ago [1]. They act by binding to the sulfonylurea receptor (SUR-1) associated with the proteic units of the K+ channel of the β-cell. This leads to the closure of the K+ -channel, an effect, which is physiologically induced by the increase of the ATP/ADP ratio resulting from the metabolism of glucose in the β-cell.(19)

**Metformin:**

Since the results of the UKPDS cohort of overweight patients, which showed a beneficial effect of metf-

ormin on cardiovascular events this drug is recommended as a first line drug therapy in the majority of type 2 diabetic patients. The major effect of metformin is the reduction of hepatic glucose production, and to a lesser extends improvement of peripheral insulin sensitivity However, despite five decades of clinical use, the mechanism of action of the drug at the molecular level remains largely unknown In recent years· it has been attributed to the stimulation of adenosine monophosphate activated protein kinase (AMPK) [2]Metformin circulates in unbound form and is eliminated by the kidney in unchanged form Clinically significant drug–drug interactions are rare, but cimetidine has been reported to reduce the renal clearance of metformine. Inversely, the co-administration with acarbose reduces the bioavailability of metformine · Overall, metformin decreases HbA1c to an extent similar to SUs (20)

**Thiazolidinedione**

The insulin sensitizing agents thiazolidinediones (TZDs) are agonists of the nuclear peroxysome proliferator activated receptor γ (PPAR-γ), which plays a major role in the metabolism of adipose tissue and indirectly controls glucose metabolism in diabetic patients by reducing free fatty acid levels and favourably altering the secretion of several adipokines involved in insulin sensitivity By contrast with metformin, TZDs act mainly at the peripheral level and to a lesser degree on hepatic glucose production.(21)

**Alpha-glucosidase inhibitors (AGI)**

Acarbose, miglitol and voglibose (not available in Europe) are competitive inhibitors of the α-glucosidases, the enzymes located in the brush border of enterocytes, which are responsible of the cleavage of saccharose, maltose, maltotriose and several other oligosaccharides. This inhibitory effect delays glucose absorption and consequently decreases the post-prandial glucose peak and insulin response to the meal Acarbose a pseudotetrasaccharide, is partly degraded in the bowel and some of its fragments are absorbed and eliminated in urine, while miglitol is totally absorbed and eliminated in unchanged form in urine(21)

- **Herbal treatment of diabetes:**

In the last many decadeseco-friendly,bio-friendly, cost effective and fairly safe, factory- grounded drugs have moved from the borderline to the main sluice with the increased exploration in the field of traditional drug. There are several literature reviews by different authors aboutanti-diabetic herbal agents, but the most instructional is the review by Attaar Rahman who has proved further than 300 factory species accepted for their hypoglycaemic parcels. This review has classified the shops according to their botanical name, country of origin; corridor used and nature of active agents. One similar factory is Momordica charantia( Family Cucurbitaceae) WHO has listed 21,000 shops, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest patron of medicinal sauces and is called the botanical theater of the world(21)

**Comorbidity of diabetic:**

Some comorbid diseases such as cardiovascular disease (CVD) and retinopathy , are known to be associated with diabetes due to their shared pathophysiological profile and as such are incorporated into diabetes management programs and clinical guidelines. However, there is limited guidance to facilitate the care of concomitant non-related diseases in the diabetic patient (12)and failure to adequately do so

may result in ineffective control of diabetes-specific risk factors and may lead to decreased patient quality of life, functioning and potentially increased mortality risk. The major challenge for both the physician and patients is how to best integrate, coordinate and prioritise treatment strategies for all comorbidities, in addition to patient specific diabetes treatment goals (21)

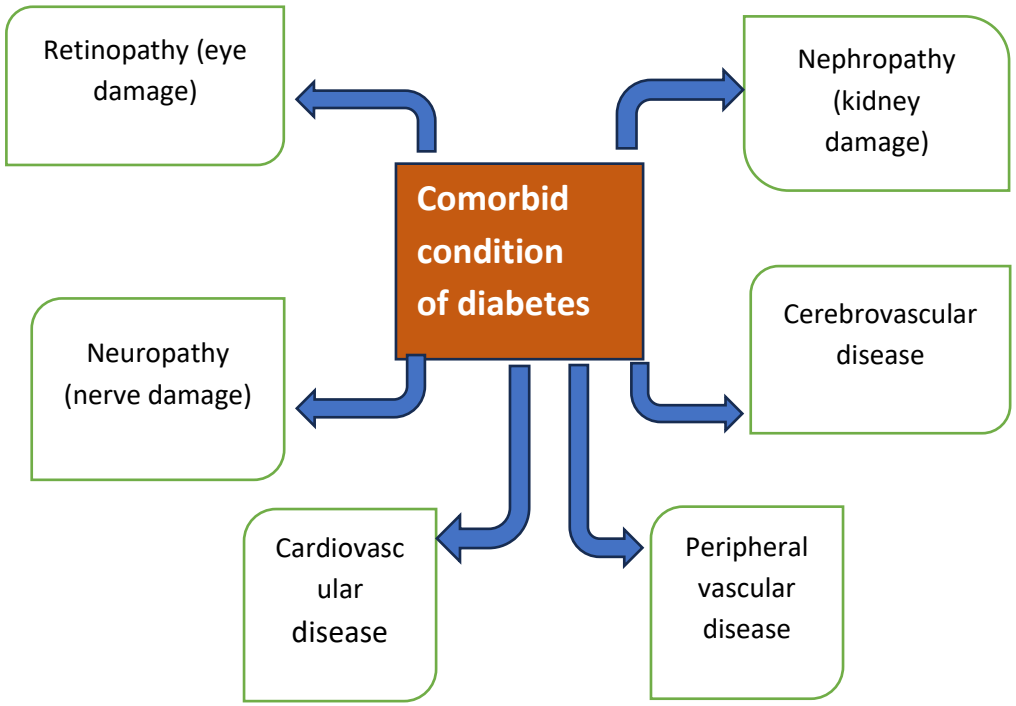



**Fig: 5 comorbid conditions of diabetes**

**Ascertainment of diabetes and comorbidities**

The primary outgrowth was the frequence of diabetes and comorbid heart complaint, hypertension, or hyperlipidemia stratified by physical exertion and BMI. The current analysis used tone- reported information performing from the MEPS- HC check, in which repliers were asked the following if they had ever been diagnosed as having diabetes( banning gravid diabetes), if they had been told on two or further different medical visits that they had high blood pressure, if they had ever been diagnosed as having coronary heart complaint, if they had ever been diagnosed as having angina or angina pectoris, if they had ever been diagnosed as having a heart attack or myocardial infarction, and if they had ever been diagnosed with any other kind of heart complaint or condition. individualities who responded appreciatively to questions regarding coronary heart complaint, angina, heart attack, or other heart complaint were classified as having heart complaint. In addition, MEPS counterplotted medical conditions to 3- number ICD- 9 canons grounded on medical and drugstore application and tone-report. Also, 259 mutually exclusive clinical bracket orders were counterplotted from ICD- 9 canons in order to give clinically homogenous groupings. The ICD- 9 to clinical bracket orders crosswalk is available from ( excursus 2). The current exploration used clinical bracket orders 053 " diseases of Lipid Metabolism " to identify individualities with hyperlipidemia.

**Table:1 Prevalence of diabetes comorbidities**

| Sr No | comorbidities | N | % | N | % | N | % |
|---|---|---|---|---|---|---|---|
| **1** | Hypoglycemia/Hyperglycemia | 33 | 52.4 | 46 | 48.4 | 79 | 49.7 |
| **2** | Visual problem | 03 | 4.7 | 04 | 4.2 | 07 | 4.4 |
| **3** | Renal disease | 02 | 3.2 | 01 | 1.0 | 03 | 1.9 |
| **4** | neuropathy | 13 | 20.6 | 07 | 7.4 | 20 | 12.6 |
| **5** | Hypertension | 29 | 46.0 | 46 | 48.4 | 75 | 47.2 |
| **6** | Urinary tract infection | 17 | 26.9 | 15 | 15.8 | 32 | 20.1 |
| **7** | Depression | 21 | 33.3 | 09 | 9.5 | 30 | 18.8 |
| **8** | Obesity | 33 | 52.4 | 56 | 58.9 | 89 | 55.9 |
| **9** | Heart disease | 04 | 6.3 | 02 | 2.1 | 06 | 3.7 |
| **10** | Nil | 10 | 15.9 | 11 | 11.6 | 21 | 13.2 |

- **Hypertension and hypotension**

The most stressed threat of initiating a PA authority is unforeseen death secondary to an arrhythmia or an ischemic event. unforeseen death may be more likely to do when underpinning CAD is undiagnosed, and undiagnosed CAD is particularly common in persons with diabetes mellitus . (3)As described over, the threat of an adverse cardiac event following vigorous exercise is particularly high in persons with diabetes compared with the same individualities when they've not exercised in the former hour It may be that the increased adverse events associated with vigorous Dad in persons with diabetes are related to their unhappy blood pressure response to exercise. Indeed, autonomic dysfunction constantly occurs in persons with diabetes 10 – 15 times following complaint opinion· The clinical instantiations of cardiovascular autonomic neuropathy include exercise dogmatism, intraoperative cardiovascular lability( i.e., increased cardiovascular morbidity and mortality during surgery), orthostatic hypotension, effortless myocardial ischemia, and increased threat of mortality

- **Retinopathy**

Retinopathy is a commonmicro-vascular complication of diabetes that can lead to blindness. Hyperglycemia and the associated increase in free revolutionaries appear to damage the retinal vessels over time, causing disabled blood rotation and leakage of blood and blood products into the retina( nominated background retinopathy) (22)Without aggressive treatment of hyperglycemia, retinal vessels suffer ultrastructural damage, macular edema, new vessel growth( nominated proliferative retinopathy), and ultimately retinal hemorrhage causing blindness. The effect of exercise on retinal damage in those with either background or proliferative retinopathy is unclear, but there's concern that increases in blood pressure and( or) jarring movements at the ultimate stages of complaint progression may grease retinal hemorrhage··

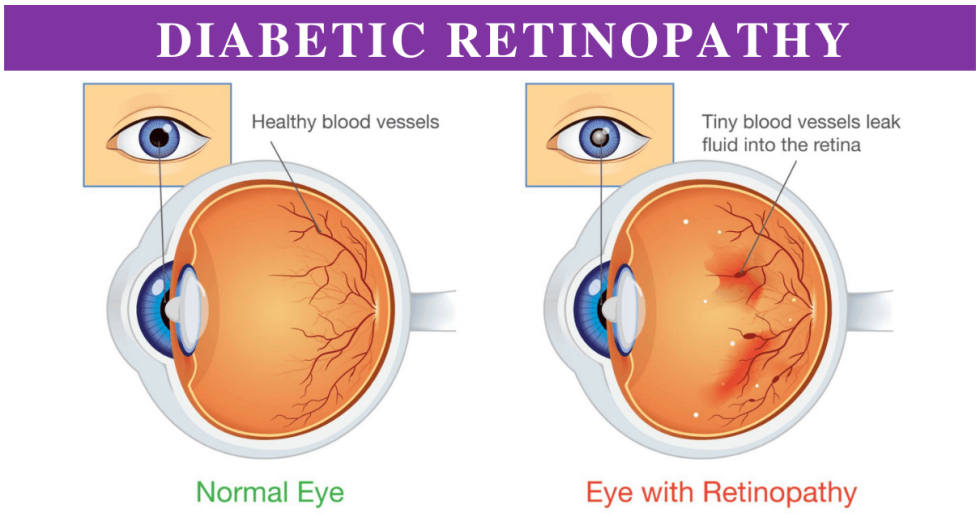
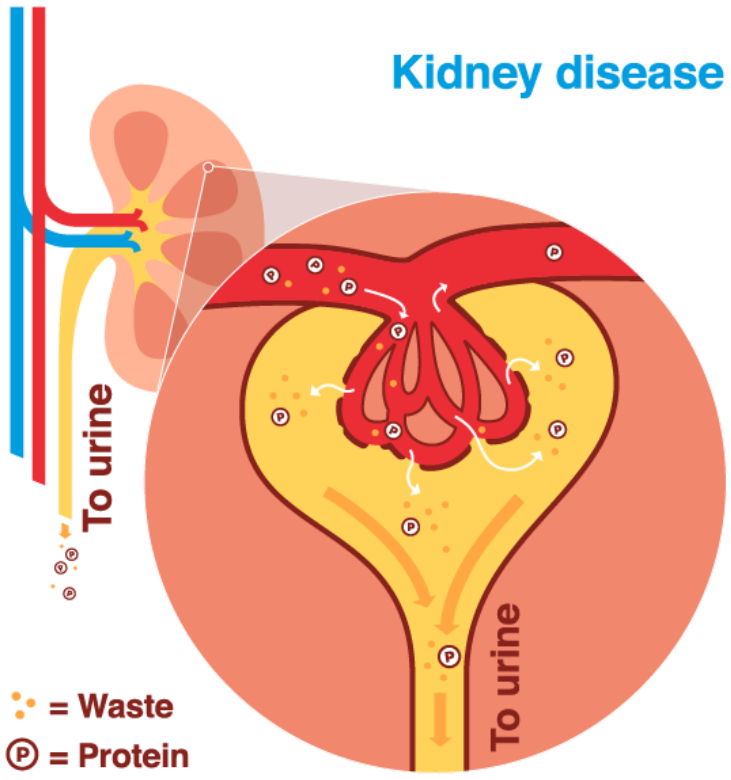



**Fig 6: diabetic retonipathy**

- **Kidney disease:**

Nephropathy (order complaint) that progresses to end- stage renal complaint is a complexmicro-vascular complication of diabetes that has a mischievous impact on a number of other systems, including muscle, cardiovascular, respiratory, nervous, gastrointestinal, urogenital, and hematological systems. Advanced nephropathy is distributed by an increase in protein loss in the order( proteinuria). We set up no substantiation that PA participation worsens resting proteinuria in persons with type 1 or type 2 diabetesDespite academic adverse goods of increased proteinuria incontinently after exercise, being data show no progression of nephropathy with exercise and, in fact, adding PA may drop being albuminuria( a type of proteinuria Incross-sectional studies, increased PA is associated with a dropped threat of developing nephropathy(23)



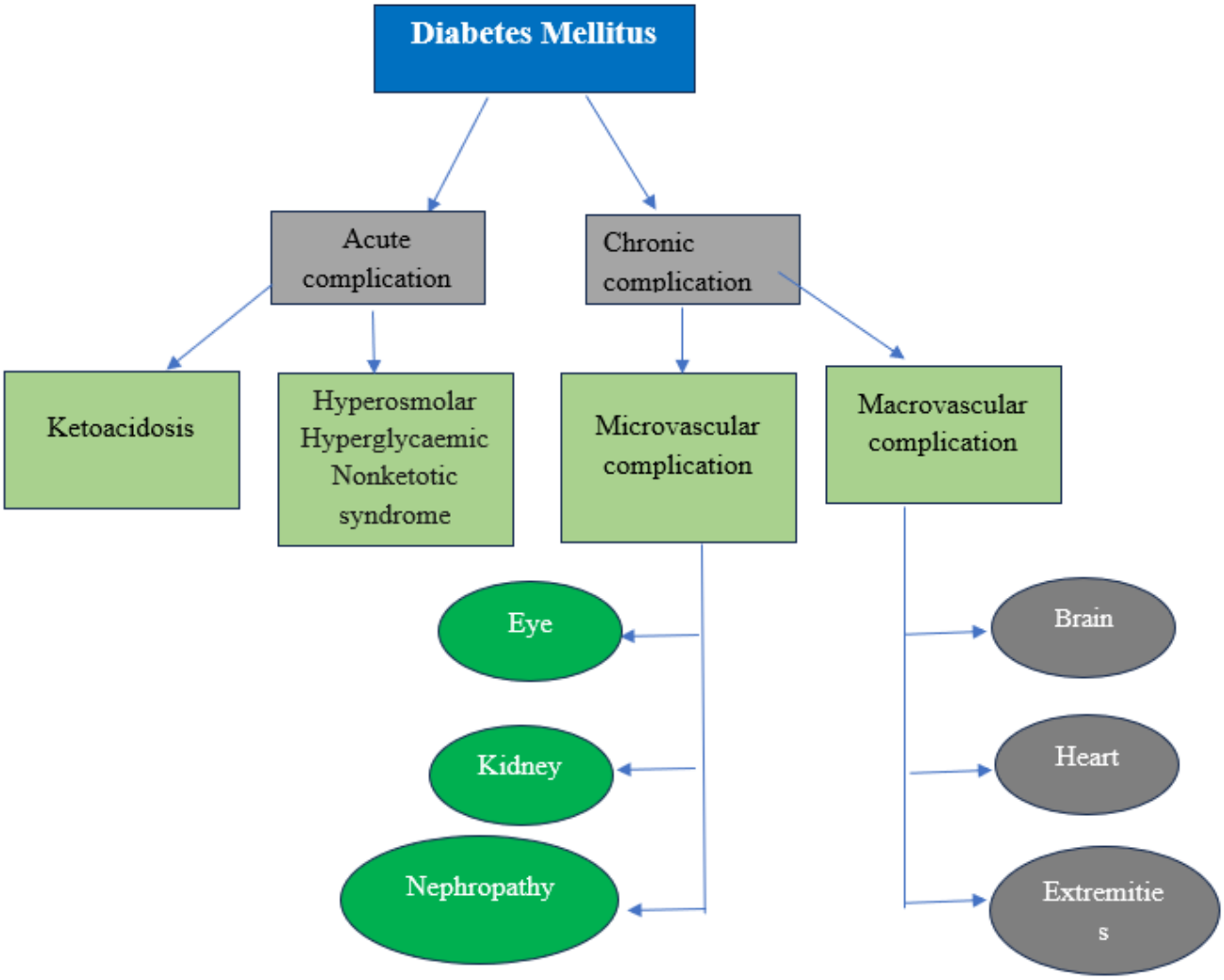



**Fig : 7 complication of diabetic mellitus**(24)

- **Sensorimotor polyneuropathy**

Diabetic peripheral polyneuropathy (i.e., disease of, or damage to, nerves outside of the brain) develops within 10 years of the onset of diabetes in 40% to 50% of people with type 1 or type 2 diabetes(23) Polyneuropathy occurs in several motor and sensory nerves and may be associated with movement difficulties, weakness, pain, and the loss of peripheral sensation that is linked to increased risk of ulceration and poor wound healing causing amputation. Both somatic and autonomic neuropathy can occur and may require referral to a specialist experienced in managing the affected body systems(24).

- **Worsening hyperglycemia**

Presently, no studies have delved if there's a minimal position of glycemic control in diabetes, as measured by HbA1c, which is demanded to insure patient safety before starting an exercise program. In cases with type 1 diabetes, acute exercise can occasionally increase blood glucose situations, although this effect is largely temporary if they're on ferocious insulin remedy(25) generally, individualities with type 2 diabetes are encouraged to initiate PA incontinently after opinion to ameliorate glycemic operation, in the absence of advanced cardiovascular complaint taking surgical intervention(15)

- **Conclusion**:

Diabetes is a very complicated disease. It is easy to diagnosis and it is difficult to treat. Laboratory plays an important part in diagnosis and care of diabetic patient its complication can be reduced through proper awareness and timely treatment. Three major complication can be related to blindness, kidney damage and heart attack. It is important to keep the blood glucose level of patient under strict control for avoiding the complication.

**Reference:**

1. Deshmukh CD, Jain A. Diabetes Mellitus : A Review. 2015;3(3):224–30.
2. Sims-robinson C, Kim B, Rosko A, Feldman EL. NIH Public Access. 2011;6(10):551–9.
3. Defronzo RA, Abdul-ghani MA. Preservation of -Cell Function: The Key to Diabetes Prevention. 2014;96(August 2011):2354–66.
4. Ifg EOF. Contributions of -Cell Dysfunction and Insulin Resistance to the Pathogenesis of. 2006;
5. Mellitus D. Annals of Internal Medicine. 2015;130(5):440–1.
6. Lebrun P, Obberghen E Van. REVIEW SOCS proteins causing trouble in insulin action. 2008;29–36.
7. Yuan M, Konstantopoulos N, Lee J. Reversal of Obesity- and Diet-Induced Insulin Resistance with Salicylates or Targeted Disruption of Ikk . 2001;293(August).
8. Kim JK, Shoelson SE, Shulman GI, Kim JK, Kim Y, Fillmore JJ, et al. Prevention of fat-induced insulin resistance by salicylate Find the latest version : Prevention of fat-induced insulin resistance by salicylate. 2001;108(3):437–46.
9. Staten MA, Shoelson SE, Targeting T. NIH Public Access. 2011;152(6):346–57.
10. Kadiki OA, Reddy MRS, Marzouk AA. Incidence of insulin-dependent diabetes ( IDDM ) and non-insulin-dependent diabetes ( NIDDM ) ( 0- 34 years at onset ) in Benghazi , Libya. 1996;32:165–73.
11. Bastaki S. Diabetes mellitus and its treatment. 2005;111–34.
12. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21(17):1–34.
13. Singh N, Kesherwani R, Tiwari AK, Kumar D. A review on diabetes mellitus. 2016;5(7):36–40.
14. Atkinson MA, Eisenbarth GS. Type 1 diabetes : new perspectives on disease pathogenesis and treatment. 2001;358:221–9.
15. Gaidhani, K. A., Harwalkar, M., Bhambere, D., & Nirgude PS. World Journal of Pharmaceutical research FORMULATION. SJIF J [Internet]. 2021;2(5):1685–703. Available from: https://hdl.handle.net/10669/87006
16. Sum C, Webster JM, Johnson AB, Catalano C, Cooper BG, Taylor R. The Effect of Intravenous Metformin on Glucose Metabolism During Hyperglycaemia in Type 2 Diabetes DT17. 1992;61–5.
17. Perriello G, Misericordia P, Volpi E, Santucci A, Santucci C, Ferrannini E, et al. Acute Antihyperglycemic Mechanisms of Metformin in NIDDM Evidence for Suppression of Lipid Oxidation and Hepatic Glucose Production. 1994;43(July).
18. Turner RC, Cull CA, Frighi V, Holman RR. Metformin , or Insulin in Patients. 2015;281(21):2005–12.
19. Aguilar-bryan L, Nichols CG, Wechsler SW, Iv JPC, Ill AEB, Gonzalez G, et al. Cloning of the P Cell High-Affinity Sulfonylurea Receptor : A Regulator of Insulin Secretion. 1995;268(April):423–

6.
20. Philipson LH, Steiner DF. Pas de Deux or More : The Sulfonylurea Receptor and K + Channels Adaptive Mutation : Who ' s Really in the Garden ? :372–3.
21. Goodarzi MO, Bryer-ash M. Metformin revisited : re-evaluation of its properties and role in the pharmacopoeia of modern antidiabetic agents. 2005;654–65.
22. Sanap GS, Sawant VA, Shende VS, Shid SL, Borkar SN, Tarannum S, et al. Anti-hyperglycemic and antioxidant activities of the Mehari choornam. Res J Pharm Technol. 2010;(2):402–5.
23. Abhijit Kumbhakar, Shaikh Suleman, Dr. Rana Zainuddin Ahmed, Kale Nitin. Topical Fibronectin Improves Wound Healing in Postmastectomy Breast Cancer Radiation Therapy : A Review. Int J Sci Res Sci Technol. 2024;11(2):469–82.
24. Vishal Dnyaneshwar Kalatre, Mrs. Nitin R. Kale, Dr Gajanan Sanap. A Review on Transdermal Drug Delivery System (TDDS). Int J Adv Res Sci Commun Technol. 2024;226–32.
25. Brar S, Sharma A. A review on medicinal herbs as immunity booster. Pharmaspire [Internet]. 2021;13(2):231–48. Available from: https://www.isfcppharmaspire.com/article_html.php?did=13795&issueno=0