

**REVIEW ON DIABETES MELLITUS ASSOCIATED HEALTH PROBLEMS
MANAGEMENT IN CLINICAL PRACTICE-A BRIEF GUIDE TO HEALTH CARE
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ABSTRACT

Diabetes mellitus associated group of metabolic diseases results in rises blood glucose levels in the body. It is a disease caused by deficiency or diminished effectiveness of endogenous insulin. The development of type 1 diabetes mellitus is based on a combination of a genetic Predisposition and an autoimmune process that results in gradual destruction of the beta cells of the pancreas, leading to absolute insulin deficiency. Type 2 diabetes mellitus is associated with excess body weight and Physical inactivity. It is caused by impaired insulin secretion and insulin resistance and has a gradual onset. Individuals with type 2 diabetes mellitus are at a significantly higher risk for coronary heart disease, Peripheral vascular disease and stroke, as well as microvascular complications affecting various organs such as eyes, kidneys and nerves. The Symptoms diabetes include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. The diabetes management through restoration of carbohydrate metabolism to a normal state. The out comes depends on relaying and targeting Pharmacological and non Pharmacological interventions and educating the Patients and community about the disease and complications will helpful for reduction in the diabetes morbidity and mortality in the community.

KEYWORDS: stroke, coronary heart disease, Peripheral vascular disease, insulin.**INTRODUCTION**

Diabetes mellitus is a chronic disease caused by inherited and acquired deficiency in production of insulin by the pancreas so the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves^[1].

The types of diabetes mellitus includes

Type 1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM).

Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM).

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels. As of 2015, an estimated 415 million people had diabetes worldwide with type 2 DM making up about 90% of the cases. This

represents 8.3% of the adult population with equal rates in both women and men^[2].

Epidemiology

The increasing prevalence of diabetes worldwide has led to a situation where approximately 360 million people had diabetes in 2011, of whom more than 95% would have had type 2 diabetes. This number is estimated to increase to 552 million by 2030 and it is thought that about half of those will be unaware of their diagnosis.^[3]

Risk factors for type 2 diabetes

- Obesity
- Lack of physical activity.
- History of gestational diabetes.
- Impaired glucose tolerance.
- Impaired fasting glucose.
- Drug therapy - eg, combined use of a thiazide diuretic with a beta-blocker.
- Low-fibre, high-glycaemic index diet.
- Metabolic syndrome.
- Polycystic ovary syndrome.
- Family history (2.4-fold increased risk for type 2 diabetes).
- Adults who had low birth weight for gestational age.

- Statins have been associated with a small, but statistically significant risk of new-onset diabetes.

Causes of Diabetes

The following factors may increase your chance of getting diabetes:

- Family history of diabetes or inherited tendency
- Being overweight
- Physical stress
- Use of certain medications, including steroid and blood pressure medications
- Autoimmune disease
- High blood pressure
- Abnormal blood cholesterol or triglyceride levels
- Age

- Alcohol
- Smoking, Pregnancy
- Pancreatic disease
- Endocrine abnormalities
- Congenital lipodystrophy.
- Genetics

Prevalence

Recently compiled data show that approximately 150 million people have diabetes mellitus worldwide, and that this number may well double by the year 2025. Much of this increase will occur in developing countries and will be due to population growth, ageing, unhealthy diets, obesity and sedentary life styles.^[4]

Diagnosis of Diabetes : Diagnostic criteria by the American Diabetes Association (ADA) include the following

WHO diabetes diagnostic criteria				
Condition	2 hour glucose	Fasting glucose	HbA _{1c}	
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %
Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥6.1(≥110) & <7.0(<126)	42-46	6.0–6.4
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)	42-46	6.0–6.4
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)	≥48	≥6.5

Pathophysiology

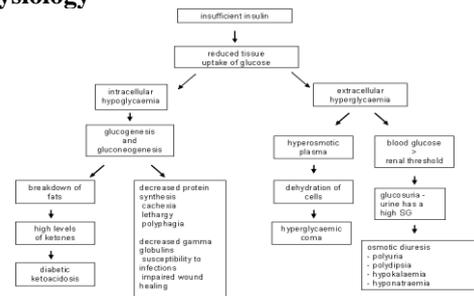


Fig 1: Pathophysiology of diabetes mellitus

Signs and symptoms

Many patients with type 2 diabetes are asymptomatic. Clinical manifestations include the following:

These symptoms might include:

- Frequent urination (polyuria) -- often at night (nocturia)
- Excessive thirst (polydipsia)
- Extreme hunger (polyphagia)
- Dry skin
- Weakness/feeling tired much of the time
- Recurring or slow-healing infections^[5]
- Weight loss (usually with high blood sugars > 300 mg/dL)
- Blurred vision
- Tingling in the hands or feet
- Nausea/vomiting (often seen in diabetic ketoacidosis in type 1 diabetes)

- Yeast infections
- Skin Infections
- Urinary tract infections



Fig 2: symptoms of diabetes mellitus

Complications linked to badly controlled diabetes

Below is a list of possible complications that can be caused by badly controlled diabetes:

Eye complications: glaucoma, cataracts, diabetic retinopathy, and some others.

Foot complications: neuropathy, ulcers, and sometimes gangrene which may require that the foot be amputated

Skin complications: people with diabetes are more susceptible to skin infections and skin disorders

Heart problems : such as ischemic heart disease, when the blood supply to the heart muscle is diminished

Hypertension : common in people with diabetes, which can raise the risk of kidney disease, eye problems, **heart attack** and stroke.^[6]

Mental health : uncontrolled diabetes raises the risk of suffering from depression, anxiety and some other mental disorders.

Hearing loss: diabetes patients have a higher risk of developing hearing problems

Gum disease: there is a much higher prevalence of gum disease among diabetes patients

Gastroparesis: the muscles of the stomach stop working properly.

Ketoacidosis: a combination of ketosis and acidosis; accumulation of ketone bodies and acidity in the blood.

Diabetic Neuropathy: diabetic neuropathy is a type of nerve damage which can lead to several different problems.

Hyperosmolar Hyperglycemic Nonketotic Syndrome:the blood glucose levels shoot up too high, and there are no ketones present in the blood or urine. It is an emergency condition.

Nephropathy: uncontrolled blood pressure can lead to kidney disease

PAD (peripheral arterial disease):The symptoms may include pain in the leg, tingling and sometimes problems walking properly.

Stroke: if blood pressure, cholesterol levels, and blood glucose levels are not controlled, the risk of stroke increases significantly.

Erectile dysfunction: male impotence.

Infections: People with badly controlled diabetes are much more susceptible to infections

Healing of wounds: cuts and lesions take much longer to heal

Need for diabetes prevention

The high economic and social costs of type 2 DM and its rising prevalence makes a compelling case for its

prevention. The Patients with established type 2 DM, intervention trials have demonstrated clear benefits of good glycaemic control in preventing or retarding the progression of microvascular complications,^[12-14] and also have reported non-significant reductions in cardiovascular disease with tight glycaemic control in subjects with type 2 DM.

Management of diabetes

Recommendations for the treatment of type 2 diabetes mellitus from the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA) place the patient's condition, desires, abilities, and tolerances at the center of the decision-making process.

The management plan for a person with diabetes includes

- Diabetes education: structured education and self-management (at diagnosis and regularly reviewed and reinforced) to promote awareness.

- Diet and lifestyle: healthy diet, weight loss if the person is overweight, smoking cessation, regular physical exercise.

- Maximising glucose control while minimising adverse effects of treatment, such as hypoglycaemia.

- Reduction of other risk factors for complications of diabetes, including the early detection and management of hypertension, drug treatment to modify lipid levels and consideration of antiplatelet therapy with aspirin.

- Monitoring and early intervention for complications of diabetes, including cardiovascular disease, feet problems, eye problems, kidney problems and neuropathy.

Pharmacological Treatment

The diabetic treatment depends on following medications were listed below

Table 1 :Diabetic drugs treatment

Subgroup	Generic name (Brand)	Route	Comments
Insulin sensitizers			
Biguanides	Metformin (Glucophage)	Oral	Weight loss No hypoglycemia GI upset
Thiazolidinediones	Rosiglitazone (Avandia) Pioglitazone (Actos)	Oral	Weight gain Peripheral edema
Insulin secretagogues			
Sulfonylureas	Chlorpropamide (Diabinese) Glibenclamide (Glyburide) Glimepiride (Amaryl) Glipizide (Glucotrol) Tolazamide (Tolinase) Tolbutamide (Orinase)	Oral	Hypoglycemia Weight gain

Glinides	Nateglinide (Starlix) Repaglinide (Prandin)	Oral	Weight gain
Alpha-glucosidase inhibitors			
	Acarbose (Precose) Miglitol (Glyset)	Oral	GI upset No hypoglycemia
Incretins			
GLP-1 receptor agonists Short-acting (4-6 hrs)	Exenatide (Byetta)	SC	Weight loss GI upset
GLP-1 receptor agonists Intermediate-acting (24 hrs)	Liraglutide (Victoza)	SC	Weight loss Nausea
GLP-1 receptor agonists Long-acting (7 days)	Exenatide ER (Bydureon) Albiglutide (Tanzeum) Dulaglutide (Trulicity)	SC	Weight loss Nausea
DPP-4 inhibitors	Sitagliptin (Januvia) Saxagliptin (Onglyza) Linagliptin (Tradjenta) Alogliptin (Nesina)	Oral	No hypoglycemia Nasopharyngitis Weight neutral
Pramlintide			
	Pramlintide (Symlin)	SC	Weight loss GI upset Adjunctive tx with insulin
Rapid-release bromocriptine			
	Bromocriptine quick-release (Cycloset)	Oral	Take within 2 hrs of awakening Nausea, stuffy nose
SGLT-2 inhibitors			
	Canagliflozin (Invokana) Dapagliflozin (Farxiga) Empagliflozin (Jardiance)	Oral	Polyuria UTIs

Insulin formulations**Table 2: Insulin Formulations**

Insulin (Brand)	Onset	Peak	Effective Duration
Rapid-acting			
Aspart (Novolog)	5-15 min	30-90 min	<5 hr
Lispro (Humalog)	5-15 min	30-90 min	<5 hr
Glulisine (Apidra)	5-15 min	30-90 min	<5 hr
Short-acting			
Regular insulin (Humulin R, Novolin R)	30-60	2-3 hr	5-8 hr

	min		
Intermediate, basal			
Insulin NPH	2-4 hr	4-10 hr	10-16 hr
Long-acting, basal			
Insulin glargine (Lantus, Toujeo, Basaglar)	2-4 hr	No peak	20-24 hr
Insulin detemir (Levemir)	3-8 hr	No peak	17-24 hr
Insulin degludec (Tresiba)	1 hr		>25 hr
Premixed			
75% Insulin lispro protamine/25% insulin lispro (Humalog mix 75/25)	5-15 min	Dual	10-16 hr
50% Insulin lispro protamine/50% insulin lispro (Humalog mix 50/50)	5-15 min	Dual	10-16 hr
70% Insulin lispro protamine/30% insulin aspart (Novolog mix 70/30)	5-15 min	Dual	10-16 hr
70% NPH insulin/30% regular	30-60 min	Dual	10-16 hr
Inhaled			
Technosphere insulin-inhalation system (Afrezza)			

Treatment regimens for diabetic therapy**Table 3: Regimens for Insulin Therapy**

Insulin Regimen	HbA1c (%)	Medication	Pattern	Diet	Lifestyle	Monitoring
Basal-only	>7.5-10	Oral medications adequately control postprandial glucose excursions	High fasting glucose with minimal glucose rise during the day	Small, regular meals; large meals will result in postprandial hyperglycemia	Reluctance to do MDI; requires oral agents	Fasting
Basal-bolus (MDI)	>7.5		Regimen can be matched to any pattern to achieve glycemic control	Regimen can be matched to any diet to achieve glycemic control	Erratic schedule, motivated to achieve tight glycemic control	Frequent blood glucose monitoring (minimum before meals and bedtime)
Once- or Twice-Daily Premixed						
Rapid-acting analogue and intermediate	>7.5	Oral agent failure (maximum tolerated dosages,	Any fasting glucose;	Large suppers, small lunches	Consistent daily routine,	Fasting and pre-supper (if insulin is

acting		contraindications, cost issues)	glucose rises during the day		reluctance to do MDI	administered twice daily)
Regular and NPH	>7.5	Oral agent failure (maximum tolerated dosages, contraindications, cost issues)	Any fasting glucose; glucose rises during the day	Isocaloric meals or larger lunches	Consistent daily routine, reluctance to do MDI	Fasting and pre-supper (if insulin is administered twice daily)

Treatment of Complications Hypertension with heart disease

These include losing weight (when needed), following the Dietary approaches to Stop Hypertension (DASH) diet, quitting smoking, limiting alcohol intake, and limiting salt intake to no more than 1,500 mg of sodium per day.

The most beneficial fall into the following categories:

There are three main types of diuretics: Potassium-sparing, thiazide, and loop.

Angiotensin-converting enzyme (ACE) inhibitors reduce the production of angiotensin, a chemical that causes arteries to narrow.

- Angiotensin-receptor blockers (ARBs) block angiotensin's action on arteries.
- Beta blockers block the effects of adrenaline and ease the heart's pumping action.
- Calcium-channel blockers (CCBs) decrease the contractions of the heart and widen blood vessels.

retina) should be sure to see an eye specialist who is experienced in the management and treatment of diabetic retinopathy. Once damage to the eye develops, laser or photocoagulation eye surgery may be needed. Laser surgery can help reduce vision loss in high-risk patients.

TREATMENT OF FOOT ULCERS

About a third of foot ulcers will heal within 20 weeks with good wound care treatments. Some treatments are as follows:

- Antibiotics are generally given. In some cases, hospitalization and intravenous antibiotics for up to 28 days may be needed for severe foot ulcers.
- In virtually all cases, wound care requires debridement, the removal of injured tissue until only healthy tissue remains. Debridement may be accomplished using chemical (enzymes), surgical, or mechanical (irrigation) means.
- Hydrogels (such as Nu-Gel), may help to soothe and heal ulcers.
- Felted foam may help heal ulcers on the sole of the foot. Felted foam uses a multi-layered foam pad over the bottom of the foot with an opening over the ulcer.
- Administering hyperbaric oxygen (oxygen given at high pressure) is showing promise in promoting healing. It is generally reserved for patients with severe, full thickness diabetic foot ulcers that have not responded to other treatments, particularly when gangrene, or an abscess, is present.
- Total-contact casting (TCC) uses a cast that is designed to match the exact contour of the foot and to distribute weight along the entire length of the foot. It is usually changed weekly. It may be helpful for ulcer healing and for Charcot foot. Although it is very effective in healing ulcers, recurrence is common.

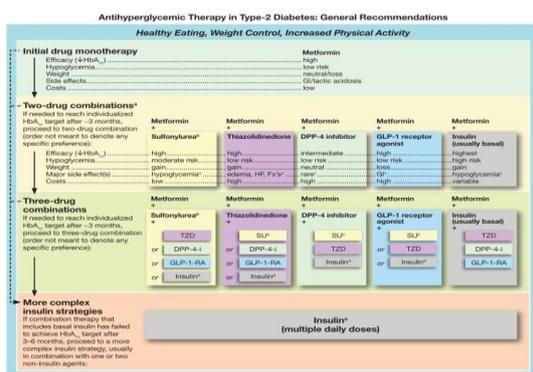


Figure 1 American Diabetes Association algorithm for the treatment of type-2 diabetes mellitus. *Consider beginning at this stage in patients with very high glycosylated hemoglobin (HbA_{1c}) (e.g., above 9%). **Consider rapid-acting, non-sulfonylurea secretagogues (meglitinides) in patients with irregular meal schedules or who develop late postprandial hyperglycemia while taking sulfonylureas. ***See Table 1 for additional potential adverse effects and risks. ****Usually a basal insulin, such as NPH, glargine (Lantus), or detemir (Levemir) in combination with non-insulin agents. *****Certain non-insulin agents may be continued with insulin; consider beginning at this stage if patient presents with severe hyperglycemia (HbA_{1c} > 10%-12%) with or without catabolic features (weight loss, ketosis). DPP-4 = dipeptidyl peptidase-4 inhibitor; Fx's = bone fractures; GI = gastrointestinal; GLP-1-RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; SU = sulfonylurea; TZD = thiazolidinedione. (Adapted with permission from Inzucchi SE, et al. Diabetes Care 2012;35:1364-1379; © American Diabetes Association.)

Fig 3: Algorithm for diabetes mellitus treatment

PREVENTION AND TREATMENT OF RETINOPATHY

Fortunately, severe and even moderate vision loss is largely preventable with tight control of blood glucose levels.

Treatment of Retinopathy: Patients with severe diabetic retinopathy or macular edema (swelling of the

TREATMENT OF NEUROPATHY

A number of different drugs are used for peripheral neuropathy pain relief: They include:

- Nonprescription analgesics, such as aspirin, acetaminophen, and non-steroidal anti-inflammatory drugs (NSAIDs). (Patients with stomach or kidney problems should check with their doctors before using these drugs.)

- Prescription painkillers, such as tramadol (Ultram). Tramadol is a drug that is similar to opioids. It can help relieve pain but has significant side effects, including nausea, constipation, and headache.
- Topical medications, particularly capsaicin (the active ingredient in hot peppers), are applied to the skin to relieve minor local pain. A 5% lidocaine patch has also shown good results in clinical trials.
- Tricyclic antidepressants, such as amitriptyline (Elavil) or doxepin (Sinequan), are effective in reducing pain from neuropathy for many patients. A combination of doxepin and capsaicin (applied to the skin) may also be helpful. Unfortunately, tricyclics may cause heart rhythm problems, so patients at risk need to be monitored carefully.
- Duloxetine (Cymbalta), a serotonin and norepinephrine reuptake inhibitor, is approved for treatment of pain associated with diabetic peripheral neuropathy.
- Anti-seizure drugs used for peripheral neuropathy pain relief include gabapentin (Neurontin), pregabalin (Lyrica), carbamazepine (Tegretol), and valproate (Depakote).

Although not proven to be beneficial, patients may also try transcutaneous electrostimulation (TENS), a treatment that involves administering mild electrical pulses to painful areas. Alternative treatments, such as hypnosis, biofeedback, relaxation techniques, and acupuncture, have also been reported to help some patients manage pain. Doctors also recommend lifestyle measures, such as walking and wearing elastic stockings.

TREATMENT OF ERECTILE DYSFUNCTION

Erectile dysfunction is also associated with neuropathy. Studies indicate that phosphodiesterase type 5 (PDE-5) drugs, such as sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis), are safe and effective, at least in the short term, for many patients with diabetes.

TREATMENT OF KIDNEY PROBLEMS

- For patients with diabetes who have microalbuminuria, the American Diabetes Association strongly recommends ACE inhibitors or ARBs. Microalbuminuria is an accumulation of protein in the blood, which can signal the onset of kidney disease (nephropathy).
- Nearly all patients who have diabetes and high blood pressure should take an ACE inhibitor (or ARB) as part of their regimen for treating their hypertension.

CONCLUSION

Diabetes is a chronic metabolic disorder and it is creating leading health problems in the community with huge social, health, and economic consequences and it is emerging as a major global health problem with the number of people living with diabetes expected to rise to 380 million by 2025. We need to follow the several health care measures required for treating the disease associated health problems. Strictly monitoring of blood

glucose levels, diet control, life style modifications, proper awareness about the disease and complications, right clinical practice, early detection and identification of risk factors, timely treatment plays a key role in the reducing the disease related burden towards in the community.

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