Exploring the Complexities ofDiabetes Mellitus: Types, Impact, and ManagementStrategies

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ABSTRACT: Diabetes mellitus is a prevalent chronic metabolic disorder characterized by elevated blood glucose levels, resulting from inadequate insulin production or ineffective utilization of insulin. This abstract provides a concise overview of diabetes mellitus, focusingon its types, causes, impact, and management strategies.

The two primary types of diabetes mellitus are type 1 and type 2. Type 1 diabetes stems from autoimmune destruction of pancreatic beta cells, leading to insulin deficiency, while type 2 diabetes involves insulin resistance and relative insulin insufficiency. Other types include gestational diabetes and rare forms like monogenic and secondary diabetes.

KEYWORDS: Diabetes mellitus, Disorder, Insulin, Types, Cells, Classification.

INTRODUCTION

Diabetes mellitus, commonly known as diabetes, is a chronic metabolic disorder that affects how our body processes glucose. It occurs when the pancreas doesn't produce enough insulin or when the body can't effectively use the insulin itproduces. This leads to elevated blood sugar levels, which can have serious health implications. Diabetes mellitus is a widespread condition that affects millions of people worldwide. In this introduction, we'll explore the causes, symptoms, types, and managementof diabetes mellitus.

DIAGNOSIS OF DIABETES

Hyperglycemia during fasting or after eating is referred to as diabetes. Diabetes mellitus (DM) is characterized by chronic hyperglycemia, which is linked to end-organ damage, malfunction, and failure in several organs and tissues such as the kidney, retina, heart, neurons, and blood vessels. According to the International Diabetes Federation (IDF), 366 million people worldwide had diabetes mellitus in 2011, and by 2030, that number is predicted to increase to 552 million (Whiting et al., 2011).The current diagnostic criteria for diabetes were released by the World Health Organisation (WHO) in a 2006 consensus statement. These criteria are consistent with the Canadian Diabetes Association (CDA) and the American Diabetes Association (ADA), as stated in their respective consensus statements (American Diabetes Association, 2010a).

These are:

- a fasting plasma glucose126 mg/dL (7.0 mmol/ L) on two occasions or more or
- a 2 hour plasma glucose200 mg/dL (11.1 mmol/ L) after 75 g glucose load (oral glucosetolerance test, OGTT) or
- a random plasma glucose200 mg/dL (11.1 mmol/L).

Haemoglobin A1c, or HbA1c, has been included by the American Diabetes Association (ADA) as a diagnostic test for diabetes mellitus (DM) as well as a gauge of the effectiveness of therapies and the management of hyperglycemia (American Diabetes Association, 2010a). The HbA1c cut-off is determined by epidemiologic studies that demonstrate a significant increase in the HbA1c range of 49–53 mmol/moL (6.6–7.0%) due to microvascular complications, specifically retinopathy (Mannarino et al., 2013). This range also aligns with the values previously mentioned for fasting, 2-hour, and random plasma glucose levels.

The combined name for impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG) is "prediabetes."

The following are the American Diabetes Association's (ADA) definitions of prediabetes: The American Diabetes Association (ADA) defines IFG as a plasma glucose level after anovernight fast that is between 100 and 125 mg/dL (5.6–6.9 mmol/L) (American Diabetes Association, 2010a). The WHO guidelines (WHO, 2006) (~110 and <126 mg/dL (~6.1 and <7.0 mmol/L)) are not met by these readings.

- A 2-hour plasma glucose level between 140 and 199 mg/dL (~7.8 and <11.0 mmol/L) after an overnight fast and a 75 g oral glucose load (HbA1C 39–46 mmol/mol (5.7–6.4%)) indicates a high risk of developing diabetes or prediabetes, according to the American Diabetes Association.

IFG and IGT can coexist, and they are linked to a higher risk of cardiovascular disease. A meta-analysis conducted in 2004 found that women had a higher risk of cardiovascular disease in IGT, with an RR of 1.36 ([95% CI, 1.23–1.52]), compared to men (Levitan et al., 2004). This slight increase in cardiovascular risk has been verified by additional, more recent meta-analyses (Ford et al., 2010).

Individuals with centripetal obesity who are diagnosed with IFG or IGT may also have concurrent abnormalities of blood pressure and cholesterol levels. The term "metabolic syndrome" has been applied to this phenomenon. According to an IDF consensus statement, central obesity is defined as waist circumference (which varies depending onethnicity; see Table 15.1) plus any two of the following factors (Alberti et al., 2006):

1. elevated triglyceride level: 150 mg/dL (1.7 mmol/ L) or treatment forhypertriglyceridemia
2. reduced HDL cholesterol: <40 mg/dL (<1.03 mmol/ L) in males and<50 mg/dL (<1.29mmol/L) in females.
3. raised blood pressure: systolic130 or diastolic85 mmHg, or treatment of previously diagnosed hypertension.
4. IFG or previously diagnosed type 2 DM.

The aim of lifestyle treatments has been to increase physical activity and achieve a 5–10% reduction in body weight. Although no discernible effect has been shown in either mortality or the prevalence of cardiovascular disease, pharmacologic intervention reduces or delays the development of diabetes in patients with IGT (American Diabetes Association, 2010a). Treatments for the several elements of this syndrome (hyperlipidemia, hypertension, and obesity) should be directed towards addressing them, and patients should get counseling ontheir increased risk of type 2 diabetes and cardiovascular disease. It is noteworthy that individuals with IGT do exhibit signs of neuropathy (Asghar et al., 2014), microalbuminuria (Singleton et al., 2003), and retinopathy. These findings should change the way we currentlyclassify and manage IGT patients.

CLASSIFICATION OF DIABETES

While type 1 and type 2 diabetes are the two main etiopathogenetic categories into which the majorityof instances of diabetes fall, some people do not fit into this strict classification. Classifying people according to the following criteria is standard clinical practice, and the categorization frequently depends on the clinical presentation at diagnosis:

1. age at onset of diabetes
2. the abruptness of hyperglycemia
3. presence of ketosis at presentation
4. degree of obesity
5. need for insulin at diagnosis.

The key is to ensure that one does not miss the diagnosis of type 1 diabetes as this has profound consequences in relation to the development of ketoacidosis and its associated mortality. Diabetic ketoacidosis (DKA) in patients with type 1 diabetes is a medical emergency that may also present with neurologic signs and symptoms. Anorexia, lethargy, thirst, polyuria, vague abdominal pain, andKussmaul respiration are followed by confusion and a decreased level of consciousness. Indeed thereis a case report of a 35-year-old male who suffered bilateral visual loss during a severe episode of DKA. Neuro-ophthalmologic examination and neuroimaging consisting of computed tomography (CT) and magnetic resonance imaging (MRI) of the brain and orbits, as well as a magnetic resonanceangiography (MRA) of brain vessels confirmed the diagnosis of bilateral posterior ischemic optic neuropathy (PION) (Smolyar and Hamrah, 2011).

Rarely, a primary central nervous system (CNS) infection, such as bacterial meningitis, accompanies diabetic ketoacidosis. Cerebral edema can complicate diabetic ketoacidosis and may present with headache, papilledema, and bilateral abducens neuropathies; it may develop on presentation or during correction of the metabolic disorder. The underlying mechanism for cerebral injury is unclear although a recent experimental study has demonstrated that both hyperglycemia and ketosis independently cause reductions in cerebral high-energy phosphates, cerebral blood flow, and cortical water distribution (Glaser et al., 2012). Secondary complications include cerebral infarction, cerebral venous sinus thrombosis, and compression neuropathies. Hyperosmolar nonketotic coma (HONK), a major metabolic complication that can cause significant neurologic deficits, is primarily seen in older patients with type 2 diabetes. A recent large case series of 51 patients admitted with HONK revealed a high mortality rate of 16%. A nonketotic hyperosmolar syndrome is characterized by blood glucose levels above 33 mmol/L (600 mg/dL) and plasma osmolarities above

320 mOsm/L without the presence of acidosis or ketonemia. Neurologic symptoms and indicators may indicate this condition in and of themselves. Neurologic symptoms include seizures, hemiplegia, aphasia, brainstem abnormalities, dystonia, chorea, and a diminished degree of consciousness. Polyuria, polydipsia, thirst, exhaustion, and generalized weakness are also frequent.In fact, the nomenclature C-H-BG (chorea, hyperglycemia, basal ganglia) syndrome is now used to describe hemiballism/hemichorea coupled with hyperglycemia (Bizet et al., 2014). Epilepsia partialis continua (EPC), for example, is a continuous form of tonic, movement-induced, or focal seizures. In fact, according to a series from India, 10 out of 17 patients who presented with EPC had HONK in the past (Shrivastava et al., 2013). Visual symptoms, hallucinations, hemichorea, tonic eye deviation, nystagmus, aberrant pupil responsiveness, and meningeal signals are examples of unusual neurologic traits. Treating hyperglycemia may be a more efficacious strategy for treating seizures than antiepileptic medication.

DIABETES TYPES

The following is a list of the common causes of diabetes:

- Type 1 diabetes is autoimmune in nature and results from a complete lack of insulin. Before diabetes mellitus was reclassified based on etiopathology, this condition was known as insulin-dependent diabetes mellitus (IDDM). The disease is characterized by immune-mediated b cell death, and hyperglycemia doesn't appear until 90% of b cells are gone.
- 90–95% of cases of diabetes are type 2 DM, which is the most prevalent type (American Diabetes Association, 2010a). Insulin resistance is the main abnormality,however it develops as a result of a relative insulin shortage.
- Gestational diabetes is a type of carbohydrate intolerance that appears or is initially diagnosed during pregnancy. Type 1 or type 2 diabetes mellitus that has never been diagnosed before can show symptoms, especially in the early stages of pregnancy. Buttype 2 diabetes and gestational diabetes are seen as distinct conditions. An increased need for insulin arises from the progression of insulin resistance during pregnancy. In the great majority of pregnancies, the demand is readily met, and the balance between insulin resistance and insulin supply ismaintained. However, if resistance becomes dominant the pregnant woman becomes hyperglycemic.
- Hyperglycemia typically appears before the age of 25, and various types of diabetes are linked to genetic abnormalities in b cell activity. These diverse individuals have little to no impairments in their ability to utilise insulin, and are known as maturity onset diabetes of the young (MODY). Since they are autosomal dominant illnesses, a family history is crucial to the diagnosis. The secretion of insulin is not working properly. Common variants of MODY include MODY2 (glucokinase defect) and MODY3 (HNF1-a defect, 1%–2% of all cases of diabetes).
- Patients with HNF1-a diabetes require early diagnosis because this type of diabetesresponds well to low-dose sulfonylurea medication. This therapy acts on the KATP channel, circumventing the mechanism causing hyperglycemia. Sulfonylureas bind to a subunit of the ATP-sensitive K+ channel and close the channel, raising the b cell's membrane potential and causing voltage-gated Ca2+ channels to open, which in turn stimulates the release of insulin. Sulfonylureas avoid the main b-cell abnormalities brought on by decreased HNF1-a function because glycolysis and mitochondrial ATP synthesis happen upstream of the sulfonylurea receptor (McKinney et al., 2004).
- Heterozygous glucokinase deficiency, or MODY2, seldom needs therapy outside of pregnancy and causes mild fasting hyperglycemia. According to Fajans et al., it is linked to a low incidence of microvascular illness.
- Two to twelve percent of cases of diabetes are caused by LADA (latent autoimmune diabetes in adults). Patients are frequently mistaken as having type 2 diabetes and are usually diagnosed after the age of 35. Sulfonylureas are initially used to establish glucose control; however, patients with this condition are typically thinner and require insulin therapy more quickly than those with type 2 diabetes (Nambam et al., 2010).
- Certain neurologic disorders are more likely to result in autoimmune-mediated diabetes, especially if autoantibodies against glutamic acid decarboxylase (GADAb) are highly prevalent. GADAb titers are exceptionally high in patients with stiff personsyndrome (SPS) and progressive

encephalomyelitis with rigidity and myoclonus (PERM). A third of those with SPS go on to acquire diabetes (Walikonis and Lennon,1998). Myotonic dystrophy, Laurence Moon-Biedl syndrome, Huntington's chorea, and Friedreich's ataxia are among the neurological conditions linked to diabetes. People who have these genetic disorders need to be regularly screened for diabetes.Point mutations in mitochondrial DNA are uncommon.

- GENERAL ASPECTS OF DIABETES MELLITUS 213 Maternally inherited diabetes and deafness (MIDD) syndrome is a diabetes and deafness-related syndromethat is based on DNA (Chen et al., 2004).
- Neuroendocrinopathies, which affect people who already have abnormalities in insulin secretion or utilization, induce diabetes by antagonistically affecting insulin through a range of hormones (growth hormone, cortisol, glucagon, epinephrine, and others). When the hormone imbalance is corrected, diabetes usually resolves.

THE DIABETIC HISTORY

A brief clinical history (Table 15.2) should be extracted so as to obtain relevant information that is of benefit in management. As previously described, the mnemonic Diagnosis, Control, Complications, Teachable Issues (DCCT) based on the landmark study can assist with an organised assessment (Zochodne et al., 2010).

GLYCEMIC GOALS

The landmark studies on type 1 diabetes (DCCT, 1995) and type 2 diabetes (UKPDS, 1995) showhow important glycemic management is in slowing the development of diabetic microvascular and other complications. The American Diabetes Association (ADA) recommends that nonpregnant persons aim for a HbA1c target of less than 53 mmol/mol (7%) unless there is a compelling reason,such as hypoglycemia unawareness (American Diabetes Association, 2010b).

MEDICATION FOR DIABETES

There are several ways to treat hyperglycemia, and the pathology and patient presentation will determine when to start treatment. Insulin will unavoidably be needed right away by those with type 1diabetes. The choice of insulin, oral hypoglycemic medications, and regimens for type 2 diabetes is complicated and depends on a number of factors, including cost, side effect profile, pharmacological efficacy, dose regimens, specific contraindications, and drug interactions. Metformin medication is regarded as the first-line treatment for type 2 diabetes mellitus, and it typically needs a time of lifestyle adjustment.

AN ALGORITHM FOR THE MANAGEMENT OF NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS.

According to Nathan et al. (2009), the ADA consensus statement serves as the foundation for the type 2 diabetes treatment protocol shown in Figure 1. This gives the basic instructions for starting diabetes therapy. In the UKPDS, metformin was reported to significantly lower glycemia and to decrease the incidence of cardiovascular events and hypoglycemic episodes (UK Prospective Diabetes Study Group, 1998a). Metformin is now recognised as the first-line treatment for type 2 diabetes. Moreover,careful blood pressure management decreased the frequency of macrovascular and microvascular events (UK Prospective Diabetes Study Group, 1998b), emphasising the importance of comprehensive medical treatment.

Clinical history		
Diagnosis		Year of diagnosis
		Duration of preceding symptoms
		Classical history of type 1 versus type 2 DM (ketotic versus nonketotic presentation)
		Family history. Maturity onset diabetes of the young (MODY)
Control	Monitoring of hyperglycemia	Home capillary blood glucose readings and HbA1c. Monitor trends of CBG and HbA1c
	Drug therapy	Insulin/oral agents – types, frequency, adherence, side-effects, insulin injection sites for lipohypertrophy, dietary advice
	Hypoglycemia	Frequency of episodes. Hypoglycaemic awareness/unawareness. Effect on occupation/driving. Need for a medic alert bracelet
Complications	Microvascular	Previous fundoscopy/retinal screening. Previous ophthalmology exams, photocoagulation scars
		Known renal disease/previous screening for renal disease with 24 hour urinary protein collections or albumin-creatinine ratio (ACR)
	Macrovascular	Ischemic heart disease, peripheral vascular disease
		Transient ischemic attack, cerebrovascular accident
		Renovascular hypertension through renal artery stenosis
	Neuropathy	Sensory loss, muscle wasting, limb extremity pain, early satiety, gustatory sweating, diarrhea, abdominal bloating, postural symptoms, erectile dysfunction
	Associated conditions	Hypertension
		Hyperlipidemia
		Autoimmune disorders
		Screening for sleep apnea in the obese patient – Epworth score
Teachable issues	Lifestyle modification	Smoking cessation, weight loss, alcohol reduction
	Psychological	Stressors, depression
	Fertility/antenatal support	Both men and women (Holstein et al., 2012)
	Insight into diabetes	Medication use and side-effects
		Prevention of hypoglycemia/hyperglycemia
		Metabolic targets and monitoring of capillary glucose

FIGURE 1. Alam, U., Asghar, O., Azmi, S., & Malik, R. A. (2014). General aspects of diabetes mellitus. *Handbook of clinical neurology*, *126*, 211-222.

Oral hypoglycemic agents and insulin in type 2 diabetes mellitus

Since a reasonable quantity of endogenous insulin is produced, oral hypoglycemic medications operate under the assumption that this is the case. As a result, the goalof oral therapies is to modify insulin release or sensitivity. Nevertheless, in type 2 diabetes, insulin therapy by itself does not alter the underlying pathophysiology of insulin resistance. Through a decrease in b cell mass, b cell dysfunction, and pancreatic islet amyloid deposition, this pathologic process leads to a progressive loss in b cells (Porte and Kahn, 2001). Combining insulin and oral medications may increase effectiveness while having less detrimental effects on weight gain.
Combining insulin and metformin may help reduce weight gain, lower insulin dosages, and improve glycemic control, according to a prior assessment of combination treatments for type 2 diabetes (Yki-Jarvinen,2001).

Insulin in type 2 diabetes mellitus

Although it is outside the purview of this review, a thorough analysis of insulin regimens and kinds will be briefly discussed. In addition to oral medication, which commonly consists of metformin, a once-daily dose of long-acting insulin, or insulinglargine, may be administered. The purpose of this combination is to prevent nocturnal hepatic gluconeogenesis-induced overnight hyperglycemia.

Below is a list of additional frequently utilised regimens:

- Premixed insulin (usually 30% short acting and 70% long acting) twice a day.Guidelines for the administration of insulin analogues or premix insulins in type 2 diabetes have been established by prior research.
- The use of once-daily aspart premix 70/30 to reach the target HbA1c with the potential to increase injection frequency was evaluated in the 1-2-3 Study (Raskin et al., 2005). In this study, if HbA1c targets were not reached, 12 units of premixed aspart 70/30 insulin were started at midday or with the largest meal of the day. If this wasn't enough, insulin was then administered more frequently with meals. In comparison to once daily glargine, this regimen was more successful in reaching HbA1c objectives. If not, the usual regimen of twice-daily premixed insulin

is two-thirds and one-third of the total.An approximate total daily dose of insulin is based on 70% of the patient body weight in kilograms.

- Basal bolus regimen of multiple injections of short acting or prandial (meal time) insulin with a single daily dose of intermediate or long acting insulin. This provides the greatest flexibility as patients can match the insulin requirement to food intake. A reasonable initial prandial short acting insulin dose is 4–6 units before eachmeal with a long acting insulin, e.g., Lantus, at 1/5 body weight of the patient. Thus apatient weighing 75 kg would initiate on 15 units of Lantus at night.
- The addition of night time long acting insulin may be preferred; however, it is now thought that loss of prandial/postprandial glucose control occurs first with sustained nocturnal hyperglycemia being possibly the later pathologic process. Thus a divergence in opinion occurs between the traditional concept of the initial addition of nighttime long acting insulin as compared to prandial insulin. Continuous glucose monitoring systems (CGMS) may be of benefit in the evaluation of hyperglycemia in these circumstances and for subsequent initiation of insulin.

Review of diabetic physical examination with associated signs of secondary diabetes

Assessment of vital signs	Hypertension or hypotension? Orthostatic vital signs may be useful in suggesting the presence of an autonomic neuropathy. A supine blood pressure and heart rate measured after 10 minutes followed by an assessment immediately after the patient arises (also describing any symptoms of dizziness) obtaining a further blood pressure and heart rate after 3 minutes
	Kussmaul breathing at presentation suggests diabetic ketoacidosis and demands an urgency in investigations and therapy, particularly the need for intravenous fluid and insulin
Secondary diabetes and associated conditions	Hemochromatosis – bronze skin coloration
	Cushing's disease/syndrome – moon face, buffalo hump, abdominal striae, centripetal obesity
	Acromegaly – rognathism, macroglossia, dental splaying, prominent frontal-orbital ridges, spade-shaped "doughy" hands
	Polycystic ovarian syndrome – hirsutism, skin tags, acanthosis nigricans
	Diabetes associated with neurological syndromes – deafness, ataxia, myopathy
	Obesity – BMI
Fundoscopic examination	Fundoscopic examination should include visualization of the whole retina (by pharmacologic dilatation of the pupil if feasible) to include the optic disc, macula and vessels
	If hemorrhages or exudates are seen, particularly within one disc diameter of the macula, the patient should be referred to an ophthalmologist on an urgent basis
Foot examination	Assessment of feet for deformity, ulcers, fissuring
	Palpation of dorsalis pedis and posterior tibialis pulses
	Assessment of peripheral sensory neuropathy with advice for foot care if found. This highlights the importance of foot care for the prevention of foot ulcers and ultimately lower extremity amputation. Sensory examination of the feet and check for knee and ankle deep tendon reflexes
Vascular assessment	Peripheral vascular examination – radial, ulnar, brachial, femoral, popliteal, dorsalis pedis and posterior tibialis
	Carotid, renal and femoral bruits
Skin	Diabetic dermopathy – well-circumscribed, small, round, hyperpigmented lesions mainly found on the anterior tibial surface of the lower leg
	Necrobiosis lipodica diabeticorum – yellow, depressed atrophic plaques on the anterior tibial surface of the lower leg which ulcerate with trauma
	Acanthosis nigricans – thick, velvety darkened patches on the neck and axilla
	Granuloma annulare – reddish bumps arranged in a circle or ring over the backs of the forearms, hands or feet
Other examinations	Gastric succussion splash – delayed gastric emptying (gastroparesis)
	Testicular examination – testicular atrophy and diabetes-associated hypogonadism
	Insulin administration sites – lipohypertrophy and lipoatrophy

Figure 2.: Alam, U., Asghar, O., Azmi, S., & Malik, R. A. (2014). General aspects of diabetes mellitus. *Handbook of clinical neurology*, *126*, 211-222.

Insulin in type 1 diabetes mellitus

Initiating insulin in type 1 DM is somewhat simpler primarily due to the mode of presentation in which ketoacidosis is predominant. Total insulin requirements over 24 hours by intravenous insulin infusions once the anion gap and severe hyperglycemia (in ketoacidosis) have normalized gives an adequate indication of the subsequent total subcutaneous insulin needed. Common regimens are as below with twice daily premixed insulin and basal bolus regimens predominating. Additional oral therapy has no role in the treatment of type 1 DM, although the use of metformin in overweight individuals with type 1 diabetes is of benefit.Types of insulin therapies are detailed in fig. 4.(Alam et. al.

2014).

Oral antihyperglycemic agents

Drug class	Name and dose	Mechanism	Advantages	Disadvantages
Biguanides	Metformin max 2500 mg daily Usual dose 1 g twice daily	Reduction in hepatic gluconeogenesis and increased peripheral glucose utilization	Weight neutral, lack of hypoglycemic episodes, cardioprotective, cheap	Gastrointestinal side-effects, contraindicated with renal impairment (eGFR < 30 mL/h)
Sulfonylureas	Gliclazide max 320 mg daily Glibenclamide max 15 mg daily Glimepiride max 4 mg daily Glipizide max 15 mg daily Gliquidone max 180 mg daily	Stimulate insulin secretion	Rapidly effective, relatively cheap	Weight gain, hypoglycemia, may potentiate increased progressive β cell failure
DPP-IV inhibitors	Sitagliptin 25–100 mg once daily Vildagliptin 50 mg twice daily Saxagliptin 2.5–10 mg once daily Linagliptin 5 mg once daily (no need for dose adjustment in hepatic and renal impairment)	Inhibition of DPP-IV and increase in endogenous GLP-1	Weight neutral, lack of hypoglycemic episodes	Long-term safety not established, possible propensity for Upper Respiratory Tract Infection (URTI), expensive, contraindicated with renal impairment (eGFR < 50 mL/h although may be reduced in the future for saxagliptin as it is both hepatically and renally metabolized)
Glitazones	Pioglitazone* max 45 mg daily	Increase insulin sensitivity through PPAR-γ receptors	Improved lipid profile potential decrease in myocardial infarction	Fluid retention, congestive heart failure, weight gain, anemia, bone fractures, expensive, **possible association with bladder neoplasm**
GLP-1 analogs	Exenatide Max 10mcg BD Liraglutide Max 1.8 mcg OD ByDureon 2 mg Weekly Lixisenatide 20mcg OD	GLP-1 analogs bind to their respective receptor on the pancreatic β cells and enhance glucose-mediated insulin secretion. Glucagon secretion is suppressed and gastric motility is delayed	Weight loss, improved lipid parameters and blood pressure	Requires injection, Frequent gastrointestinal side-effects, long-term safety not established, can potentiate hypoglycemia with concurrent sulfonylurea or insulin use
Amylinomimetic	Pramlintide 120mcg TDS with meals	Delayed gastric emptying, inhibitory to glucagon synthesis and reduces postprandial glucose levels	Weight loss, effective therapy in type 1 and 2 diabetes	Requires injections, frequent gastrointestinal side-effects, long-term safety not established
SGLT2 inhibitors	Canagliflozin 100-300 mg per day Dapagliflozin 5/10 mg OD Empagliflozin 10/25 mg OD	Inhibits SGLT2 transport of sodium and glucose in the proximal renal tubule cells promoting renal excretion of glucose	Weight loss, improved lipid parameters and blood pressure	Urinary tract infection and genital infections such as candidiasis, increased thrombophilia risk on initiation. Not recommend for use with pioglitazone (theoretical bladder cancer risk) and GLP-1 mimetics (no trial data). Dose adjustment or discontinuation required with declining eGFR required
Meglitinides	Nateglinide 60-180 mg TDS with meals Repaglinide 500mcg TDS upto 4 g TDS (max) with meals Mitiglinide 10 mg TDS with meals	Bind to an ATP-dependent K^+ (K_{ATP}) channel on the cell membrane of pancreatic β cells in a similar manner to sulfonylureas thus releasing (pro)insulin	Rapid onset of action and short duration of activity, and should be administered shortly before each main meal	Weight gain and hypoglycemia

Figure 3 : *Pioglitazone is currently banned in India, France, Canada, Australia, NewZealand, and Japan because of a possible association with bladder cancer.

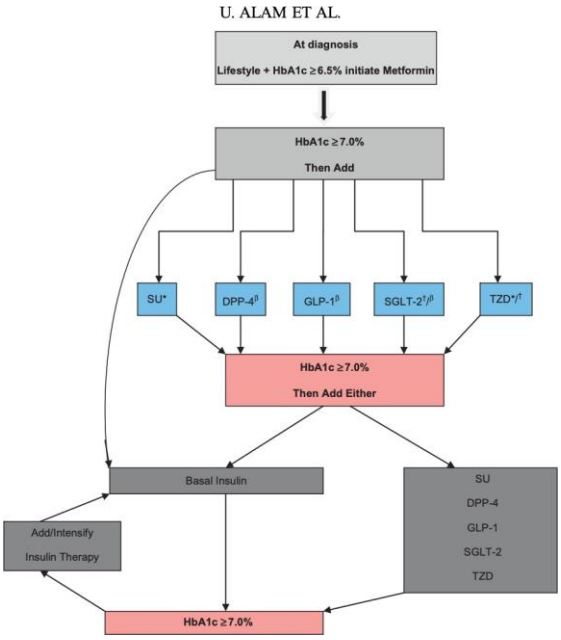

Figure 1. :Algorithm for treatment for type 2 diabetes mellitus. SU, sulphonylurea; DPP-4, dipeptidyl peptidase 4 inhibitors; GLP-1, glucagon-like peptide 1 analogue;SGLT-2, sodium-glucose co-transporter-2 inhibitor; TZD, thiazolidinediones/glitazones. *Avoid if weight gain is detrimental. {Avoid in haematuria/urinary tract malignancies. bBeneficial weight and hypoglycaemia profiles. Dapagliflozin and pioglitazone are not recommended in combination due to possible risk of urinary tract malignancies(Alam et. al. 2014).

Common forms of insulin therapy

Insulin	Brand names	Usual time of administration	Onset of action	Notes
Rapid acting	Humalog, Novolog, Apidra	Premeal	10–30 min	
Short acting	Humalog	Premeal	30 min – 1 h	
Intermediate acting	NPH, Lente, Humulin I, Insulatard	Commonly twice daily premeals	1–2 h	Usually combined with rapid-acting insulin
Long acting	Levemir, Lantus, Tresiba, Ultralente	Once daily (usually bedtime)	30 min – 3 h	Often combined with rapid-acting insulin
Premixed	Mixtard 10-50*, Humulin M3, Humalog 25, 50, Novomix 30	Twice daily premeals	As per constituent insulin	These are combinations of specific proportions of intermediate-acting and short acting insulin without multiple injections. Hence these regimens are convenient

*Mixtard 30 has been withdrawn by Novo Nordisk.

Figure 4. : Alam, U., Asghar, O., Azmi, S., & Malik, R. A. (2014). General aspects of diabetes mellitus. *Handbook of clinical neurology*, *126*, 211-222.

DIABETES CONTROL OF INPATIENTS

No matter what the reason, hyperglycemia in hospitalised patients is linked to poor clinical outcomes (Moghissi et al., 2009). All doctors who treat inpatients will be impacted by the rising diabetes epidemic. According to an economic analysis conducted in the United Statesin 2007, people with diabetes accounted for 22% of inpatient hospital days (American Diabetes Association, 2008). Several variables make controlling hyperglycemia during hospital stays difficult. These include irregular food and patterns, inactivity, illness, infection, and concurrent medication, such as b-agonists, quinolones, and corticosteroids. It is definitely not advised to drastically lower a patient's insulin when they are first admitted to the hospital, as any decrease in activity is usually more than offset by coexisting conditions. In 2009, the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE) released a joint consensus statement (Moghissi et al., 2009) that offers recommendations and a thorough summary of the literature regarding the management of glycemic control in inpatient settings.

Few randomised controlled trials (RCTs) have been conducted on patients in non-intensive care units (ICUs); yet, observational studies have demonstrated significant correlations that point to poor clinical outcomes when hyperglycemia is present (Moghissi et al., 2009). which offers suggestions and a thorough summary of the research on the administration of glycemic control during hospital stays.

Few randomised controlled trials (RCTs) have been conducted on patients in non-intensive care units (ICUs); yet, observational studies have demonstrated significant correlations that point to poor clinical outcomes when hyperglycemia is present (Moghissi et al., 2009). There is only one significant study evaluating the effects of hyperglycemia in people with neurologicconditions. In a research by Pasternak et al. (2008), patients following cerebral aneurysm surgery who also had hyperglycemia and a subarachnoid haemorrhage at three months exhibited deficits in neurologic function and poorer cognitive function.

In critically sick patients, very strict glycemic control (80–110 mg/dL; 4.4–6.1 mmol/L) has proven to be a more controversial method because there hasn't been a consistent decrease in mortality; rather, severe hypoglycemia has become more common (Wiener et al., 2008). The current recommendation is to maintain a glucose range of 140–180 mg/dL (7.8–10.0 mmol/L) once insulin has been initiated in critically ill patients (e.g., hemodynamic compromise, fluctuating consciousness, potential for rapid deterioration, etc.). Continuous intravenous insulin infusion is the most effective method in achieving glycemic targets (Moghissi et al., 2009).

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