

QUARTERLY MEDICAL REVIEW

Vol.54, No. 4

October - December 2003

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DIABETES MELLITUS (Part 2)

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MONITORING GLYCEMIC CONTROL

The importance of glycemic control is no longer a controversial issue as it has been conclusively proved in both type 1 and type 2 diabetics by Diabetes Control and Complications Trial, Kumamoto and UKPDS studies. As hyperglycemia is strongly associated with the development and progression of diabetic complications, the importance of accurate monitoring of glycemic control cannot be overemphasized. The different parameters are listed in Table 1

TABLE 1 : Monitoring and Follow up of Diabetes

<ul style="list-style-type: none"> ◆ Urine Glucose has limitations, do not use alone ◆ Blood sugar-FPG & 2 hr PPPG ◆ SMBG- frequency & timing-individuals needs goals ◆ HbA1c every 3-6 months ◆ Clinical exam - Every visit - minimum 3 months Optimising Wt, Blood pressure, lipids ◆ Screening for long term complications like retinopathy, nephropathy, PVD ◆ Encourage Foot care ◆ Discourage tobacco use ◆ Children - growth
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Urine Glucose Testing (No Role)

Although urine glucose testing is painless and much cheaper than blood glucose testing, it is misleading and therefore not recommended for routine use. It has limited role in the present day management strategy for diabetes. However, some diabetic patients continue to use urine testing. It can be considered as an alternative for monitoring their glycemic status since some monitoring is better than no monitoring. Test strips that quantify urine glucose should be used to avoid a false positive result. The urine glucose testing should be done in the postprandial state in a second voided specimen, so that a negative result during this state indicates adequate glycemic control. One should watch for hypoglycemia in such situations.

Urine Ketone Testing:

Urine ketone testing is indicated in the following clinical situations namely, at onset of diabetes in all young patients with diabetes, during periods of poor metabolic control (blood glucose > 250 mg/dl), during acute illness and stress, food deprivation (starvation), pregnancy (early morning sample) and when symptoms of ketoacidosis are present (such as nausea, vomiting and abdominal pain).

Urine Albumin Testing

Urine albumin provides a fair indication of kidney status. If urine albumin is negative, microalbuminuria should be tested every year.

Blood Glucose Testing:

Measurement of plasma glucose is required for initial diagnosis of diabetes. Subsequently, it is done for monitoring the adequacy of therapy. The frequency of testing depends upon the type of diabetes and the therapy used. Ideally both FPG and PPG should be measured. Monitoring must be done with the usual diet and drug intake. Extra diet or heavy diet should not replace the normal diet during monitoring. Oral glucose challenge is not required during monitoring. The standards for glycemic control are summarized in Table 2.

i. Recommended Frequency for Plasma Glucose Measurements

- The measurement of FPG and 2 hr PPG on a weekly or fortnightly basis at start of therapy. This is to be followed by monthly measurements once satisfactory control is achieved.
- However, those patients with type 2 diabetes on insulin therapy as well as stressed subjects require more frequent plasma glucose measurements as in type 1 diabetes.

TABLE 2A : Targets for control

	Ideal	Satisfactory	Unsatisfactory
FPG mg/dl	80-110	111-125	>125
2 hr PPG mg/dl	120-140	140-180	>180
BP (mm Hg)	<130/80	<140/90	>140/90
Body Mass Index (kg/m ²)	20-23		
Waist Hip Ratio	Men < 0.90 Women < 0.85		

TABLE 2B : Targets for control

	Ideal
Total Cholesterol	<180mg/dl
HDL-C	>45mg/dl
LDL-C	<100mg/dl
Triglycerides	<150mg/dl

ii. Self Monitoring of Blood Glucose (SMBG)

Ideally Self monitoring should be done by every patient as it is therapeutic. However due to cost limitation it is not routinely advised.

Indications for SMBG in clinical practice are listed in Table 3.

TABLE 3 : Indications for SMBG

Type 2 diabetes with altered renal threshold, advanced chronic complications and during period of acute stress
Peri-operative state
Labile/Brittle diabetes
Neuroglycopenia without warning, nocturnal hypoglycemia
Prone to ketosis
Pregnancy, acute infection and myocardial infarction
All cases on intensive insulin therapy

How to use Glucose Monitor

- Blood glucose monitoring systems are very easy to use and provide accurate and reliable results. These systems include a meter, test strips, adjustable blood sampler & Lancets.
- A test strip has a special ‘test area’ on one end and on this test area, there are enzymes (biochemical agents) that are similar to the ones that are used in a laboratory to test blood glucose.
- The procedure is very simple. One has to insert a test strip in a meter and with the help of the blood sampler, prick the finger to get one little drop of blood on the test area and in a few seconds the meter gives the results.
- Some meters can also automatically store the results in memory and these forms an important basis for the doctor to modify the treatment plan for the patient.
- Cutting of the strips should be discouraged.
- Periodically compare the results of patient’s with simultaneous laboratory testing.

How to get good blood sample for SMBG

Measuring blood glucose means one needs to actually get a blood sample, through painless pricking methods through modern adjustable blood sampler (Penlet) and very fine gauge sterile Lancets. The penlets have an adjustable depth setting that make finger pricks virtually painless.

One can get a good blood sample by following simple steps:

- ◆ Insert a lancet in the adjustable blood sampler.
- ◆ Adjust puncture depth.
- ◆ Cock the Sampler.
- ◆ Gently rub washed and dry hands.
- ◆ Get a drop of blood from one of the fingers using the lancet-penet
- ◆ Remove / dispose the lancet

Glycosylated Hemoglobin Testing

Glycated proteins such as hemoglobin and serum proteins provide measures of glycemia over an extended period of time depending on their half life in the circulation.

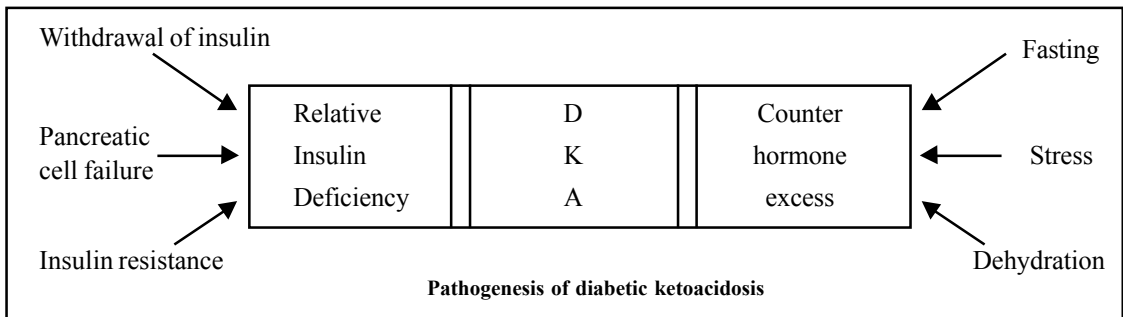
Glycosylated Hemoglobin

The degree of hemoglobin glycation is proportional to the ambient glucose concentration and is a measure of the average glycemia over the preceding three months. HbA_{1c} is the most abundant and correlates best with the degree of glycemia. Various factors can alter the HbA_{1c} levels. Falsely high values are observed in situations of increased fetal hemoglobin and uremia whereas falsely low values are observed in hemoglobinopathies and hemolytic anaemia. A change in HbA_{1c} of 1% would reflect a blood glucose alteration of about 30 mg%. Testing should be performed routinely in all patients at diagnosis and then every three months subsequently. Some other tests done are glycated albumin, fructosamine etc.

COMPLICATIONS

Acute Metabolic Complications: Diabetic Ketoacidosis (DKA)

Diabetic ketoacidosis is an important cause of morbidity and mortality amongst diabetics. It is a life threatening situation, awareness, early diagnosis and efficient management are necessary to reduce mortality. In a good centre, mortality should not be more than 5% which could be mainly due to underlying precipitating factors like myocardial infarction or severe fulminant infections. DKA develops in situations where there is relative insulin deficiency and there is counter hormone excess (Box Below). The Precipitating factors are Infection, Omission of insulin, Unknown cause and Stressful situations like, acute myocardial infarction, Cerebrovascular accident, Surgery, Trauma etc. The signs and symptoms are listed in Table 4.



Treatment

The treatment of ketoacidosis aims to correct dehydration, avoid hyper- and hypokalemia and lower blood glucose concentration. The acidosis is usually corrected by these measures and specific therapy for this is seldom needed.

Administration of insulin and replacement of fluids, including electrolytes and glucose, are the cornerstones of the treatment of DKA. During treatment, vital signs of the patient should be observed closely and timed urine flow and amounts of infusions must be recorded. The use of a flow sheet on a timed scale should be maintained.

TABLE 4 : Signs and symptoms of DKA

Symptoms	Signs
Polyuria	Hyperpnea
Polydipsia	Hypothermia
Weakness	Acetone breath
Lethargy	Acidotic breathing
Myalgia	Dyspnea
Headache	Acute abdomen
Anorexia	Dehydration
Nausea	Hyporeflexia
Vomiting	Hypotonia
Abdominal pain	Stupor/coma
Breathlessness	

If a precipitating cause of DKA (such as an infection or myocardial infarction) is detected, its treatment should be started alongwith the treatment of DKA.

In an unconscious patient, a nasogastric tube should be inserted to keep the stomach empty and prevent aspiration of gastric contents.

Correction of Dehydration : Fluid and Electrolytes

Normal saline is the fluid of choice for initial rehydration. On an average -

- * One litre should be infused in the first hour
- * Next one litre in the next 2 hrs.
- * Two litres in the next 4 hrs.
- * Two litres in the next 8 hrs.
- * i.e. 4-6 litres in 24 hrs.

The effect of saline should be monitored by blood pressure, CVP, pulse, neck veins, skin turgor. In a situation where serum sodium is 150 mEq/L, hypotonic or half normal saline may be used. When the blood glucose concentration reaches 250 mg/dl, the fluid should be changed to 5% dextrose-saline with concurrent administration of insulin, in order to avoid hypoglycemia. It takes longer for acidosis to get corrected than blood glucose.

Fluid Overload

Care should be taken not to infuse a large amount of fluid too rapidly in elderly patients, in those with existing heart disease especially congestive cardiac failure and in patients with renal failure.

Potassium Replacement

The plasma potassium may initially be high in the presence of acidosis. It begins to fall as DKA is treated. Hypokalemia is therefore likely without potassium replacement. There is no definite guideline about when to start potassium replacement. If there is good urinary output, potassium replacement should be started early during the treatment of DKA. Potassium chloride (one ampoule, 10 mEq) should be added in the third bottle of saline. The potassium level should be evaluated every two hours or as necessary. If the response is not adequate, dose must be modified. This should be avoided in the presence of renal failure. ECG monitoring is helpful since tall T waves are indicative of hyperkalemia. Patients not responding to conventional therapy may be looked for other conditions. Ringer lactate and fructose should be avoided in DKA.

Other Electrolytes

Bicarbonate may be used in severe cases of acidosis with a pH less than 6.9, bicarbonate levels less than 5 mmol/L, patients with DKA complicating acute myocardial infarction and in patients with lactic acidosis. The risks of bicarbonate therapy are shift of oxygen dissociation curve to left, hypokalemia, and CSF dysequilibrium.

Insulin

The standard method is low dose infusion of insulin by the intravenous route after an initial bolus of insulin. If IV infusion of insulin is difficult to perform, hourly intramuscular (IM) injection of insulin is an alternative method. For an IM administration, the deltoid muscle is preferred.

IV insulin therapy is given as an initial dose of 10 units as a bolus, followed by insulin infusion at the rate of 0.1 unit/kg/hour. (50 units of insulin are to be added to 500 ml of normal saline. The infusion is to be run at the rate of 1 ml/min).

IM regime involves the use of 0.1 unit/kg/hour of insulin.

With these regimens, the plasma glucose level falls at a predictable rate of around 50 mg/hr. It usually comes down to half the initial value in 6-8 hours. If at the end of 2-3 hours, the plasma glucose values do not show a predictable fall, the dose of insulin infusion is doubled i.e. 12 units/hr. Once the plasma glucose levels come down to 250 mg%, the fluid replacement should be switched over to dextrose saline infusions. Once the sensorium improves and vomiting subsides, the patient is encouraged to take oral feeds and insulin is given by SC route 4-6 hourly depending on the glucose profile. If the patient's condition does not improve within 24 hours, evaluate for other causes of coma.

HYPEROSMOLAR NON-KETOTIC COMA (HONK)

It usually occurs in type 2 diabetics. The clinical picture is dominated by profound dehydration, without ketosis or significant acidosis. Plasma glucose levels usually exceed 600 mg/dl.

The Clinical Features are Severe hyperglycemia (plasma glucose > 600 mg/dl), Profound dehydration, Elevated osmolality (more than 320*), Absence of ketosis and Variable neurological signs.

$$\left[* \text{Osmolality} = (\text{Na}+\text{K}) \times 2 + \frac{\text{Glucose (mg\%)}}{18} + \frac{\text{Urea (mg\%)}}{3} \right]$$

The principles of treatment are similar to those of DKA. The infusion of fluid should first be with half normal saline and continued until recovery of extra- cellular fluid and good urine flow. The same scheme of insulin administration is adequate. However, the patients with HONK are more sensitive to insulin than those of DKA. As with DKA, infusion of glucose should be started when the blood glucose falls to near 250 mg/dl and the replacement of potassium should be started early in the course of treatment.

LACTIC ACIDOSIS

This uncommon condition is usually seen in patients treated with phenformin and have renal, respiratory or hepatic failure. Although the incidence of lactic acidosis is very rare in India, the recognition of this condition is very important. There is severe acidosis but ketosis and dehydration are minimal or absent. In contrast to patients with DKA very large quantities of bicarbonate are needed routinely in these cases, while little hypoglycemic therapy is required. The treatment involves 5% dextrose saline infusion and insulin. Dialysis may have a role in the management. However the mortality is very high. Since large amounts of bicarbonate are administered, potassium levels must be closely monitored.

HYPOGLYCEMIA

The term hypoglycemia refers to the clinical condition resulting from an abnormally low plasma glucose levels (< 40 mg/dl). Clinically it is characterized by varying degree of neurological dysfunction and is responsive to the administration of glucose.

The Predisposing factors are Delaying or skipping meals, Decreased carbohydrate intake, Increase in the dose of insulin or oral antidiabetic drugs, Decrease in insulin requirements (after delivery, or with the elimination of stress or control of infection, renal or hepatic insufficiency), Sick days, due to unexpected physical strain after taking insulin or oral hypoglycemic drugs, Alcohol consumption etc. Hypoglycemia needs to be treated promptly. While it is useful to document the degree of hypoglycemia, this should not delay treatment, and the general advice is “If in doubt, treat”.

Clinical Features

Rapid fall of blood glucose (as with insulin) leads to manifestations of the activation of the sympathetic nervous system while a gradual fall (as seen with OHAs) lead to the symptoms due to decreased cerebral function (Table 5).

TABLE 5 : Symptoms of hypoglycemia

Neuroglycopenic	Adrenergic
Fainting	Hunger
Yawning	Perspiration
Weakness	Rise in BP
Tingling in the fingers	Tremors
Diplopia	Headache
Hysterical behaviour	Palpitation
Disorientation	Anxiety and nervousness
Mental confusion	Weakness
Convulsions and coma	

Persistence of hypoglycemia for over six hours may lead to permanent brain damage. Recurrent attacks may also contribute to mental changes in cognitive function.

Management of Hypoglycemia:

a) The Conscious Patient

The treatment involves immediate intake of 10-20 gms of glucose or a rapidly digestible form of carbohydrate orally, followed by a snack of a more slowly digestible form of carbohydrate (equivalent to one slice of bread) to maintain normoglycemia until the next meal. If the patient is on acarbose also, then treat it with glucose.

b) The Unconscious Patient

A severe hypoglycemic episode can only be treated by intravenous glucose (50-100 ml of 25% / 50% dextrose). In unresponsive patients, parenteral glucagon (0.5-1 mg IM) should be administered. In these patients carbohydrates should be given orally as soon as the patient regains consciousness. The patient must regain consciousness within half an hour. Parenteral dexamethasone is also recommended in unresponsive patients.

It is important to follow glucose level for at least 24-48 hours in patients where hypoglycemia is induced by long acting sulphonylureas (chlorpropamide/glibenclamide) or long acting insulin (Lente/NPH). A long term glucose infusion may be necessary and the patient should be hospitalized. Occasional patient may take longer time to recover.

c) Prevention of Hypoglycemia

Education of patient and family members is a must. Education of the health care providers in terms of diagnosing diabetes, its management and also diagnosing hypoglycemic episodes early is important.

CHRONIC VASCULAR COMPLICATIONS

Macrovascular Complications: Coronary artery disease

Acute Myocardial Infarction (AMI)

In diabetics as compared to non-diabetic subjects, The incidence of myocardial infarction is around three times higher and the outcome of AMI is worse. Mortality is two times higher in pre-hospital, hospital and post-hospital periods following the episode. This is particularly so in patients below 60 years of age and in obese females; more so in those with anterior infarctions. Diabetics develop complications of myocardial infarction more often than nondiabetics. These include cardiogenic shock, CHF, conduction disturbances, etc. Congestive heart failure is seen in 44% of diabetic women and 25% of diabetic men.

Infarct sizes are relatively larger and more often anterior. Incidence of silent MI is variable but by all measures more frequent in patients with diabetes. Painless or silent infarcts occur in 20% of diabetics. Presenting features may be atypical and lead to long lag period between onset and hospitalization in the intensive coronary care unit (ICCU). An estimated 20-40% patients present with atypical features such as confusion, dyspnoea, cough, fatigue, nausea, vomiting and epigastric distress. Ketosis (2-4%) or hyperosmolar state (in elderly) may be present at admission. Sudden cardiac deaths are more common. It is preferable to perform CABG than PTCA in diabetics. A major concern in the management of AMI in patients of diabetes is to provide adequate insulin in order to restore glucose utilization and reduce lipolysis and consequent rise in circulating free fatty acids. Diabetic retinopathy is no longer a contraindication for thrombolytic therapy.

Following life saving measures including the admission to intensive coronary care unit (ICCU), specific anti-diabetic therapy has to be started on a priority basis. The infarction may be massive and post-AMI period more stormy.

Diagnosis

On arrival of the patient, random plasma glucose (RPG) is to be estimated immediately. If the patient is not a known diabetic, HbA_{1c} will distinguish between stress hyperglycemia and a diabetic. Urine has to be tested particularly for ketone bodies.

In case the plasma glucose is more than 200 mg/dl, short acting insulin is to be started, preferably by IV infusion.

Monitoring for Blood/Plasma Glucose During Infusion

Monitoring is best done at the bedside by glucose monitor. Results thus obtained will guide the rate of insulin infusion from time to time. Beyond this, regular plasma glucose monitoring along with other parameters (electrolytes and ketone bodies) should be done every 4-6 hours for further management. If the serum potassium is less than 3.5 mEq/L, potassium solution has to be added to the insulin infusion device at the rate of 20 mEq/L.

Special care has to be taken in case of ketosis, hyperosmolar coma. Nutrients (including dextrose, other resuscitation fluids and essential therapy) should be administered through different IV lines. The revival in the intensified insulin therapy for AMI originated from Diabetes Insulin - Glucose in Acute Myocardial Infarction study which achieved favourable results with administration of insulin by infusion. Insulin for first 24 hours of AMI followed by subcutaneous insulin therapy for three months improved the short and long term mortality.

CEREBROVASCULAR DISEASE: STROKE

Diabetes mellitus (chronic hyperglycemia) is an important risk factor for ischemic but not hemorrhagic stroke. The relative risk of ischemic stroke is increased on an average by 2-4 fold in the diabetic population. The type and distribution of stroke in diabetic patients are not significantly different from that of non-diabetic subjects. Further, to what extent hyperglycemia contributes to promote stroke is not certain as it is so often associated with hypertension (HTN) and dyslipidemia. Framingham study indicates increased cerebral infarction even with mild glucose intolerance. Several studies have shown an increase in short and long term morbidity/mortality in diabetics, who have stroke. Hyperglycemia has been observed to worsen the severity of the attack.

Guidelines for Treatment:

All stroke victims are likely to be dehydrated and should be started with normal saline at the admission. Random plasma glucose (RPG), glycosylated hemoglobin (HbA_{1c}), urea, creatinine, electrolytes, urine for ketones should be tested and an initial value obtained. Patient should never be put on dextrose or dextrose saline to start with. The rate and total volume of normal saline administered in each patient should be determined after considering the expected total volume loss, renal/heart status and hematocrit. Any excess fluid intake may result in development of cerebral edema. At times these patients may have complications such as hyperosmolar non-ketotic state or ketoacidosis. It is very important to note that plasma glucose should not to be allowed to fall below 160 mg/dl throughout the therapy. Hyperglycemia raises lactic acid content of cerebral ischemic tissues where as cellular damage occurs in hypoglycemia.

Alongwith maintenance of normoglycaemia, a blood pressure above 200/100 mm Hg should be controlled very gradually as acute lowering of blood pressure worsens the ischemia and total outcome of the patient. Mannitol infusion can be given.

However efforts to achieve a good metabolic control should be accompanied by an aggressive approach towards cerebral reperfusion. Cerebral infarction and hypoglycemia can manifest as stroke.

ASPIRIN THERAPY IN DIABETES

People with diabetes have a two to fourfold increase in the risk of dying from the complications of cardiovascular disease. Both men and women are at increased risk. Atherosclerosis and vascular thrombosis are major contributors, and it is generally accepted that platelets are contributory. Platelets from men and women with diabetes are often hypersensitive in vitro to platelet aggregating agents. A major mechanism is increased

production of thromboxane, a potent vasoconstrictor and platelet aggregant. Recommendations on the use of aspirin are given in Table 6.

TABLE 6 : Recommendations on the use of aspirin

<p>1. Use aspirin therapy as a secondary prevention strategy in diabetic men and women who have evidence of large vessel disease. This includes diabetic men and women with a history of myocardial infarction, vascular bypass procedure, stroke or transient ischemic attack, peripheral vascular disease, claudication, and/or angina.</p>
<p>2. In addition to treating the primary cardiovascular risk factor(s) identified, consider aspirin therapy as a primary prevention strategy in high-risk men and women with type 1 or type 2 diabetes. This includes diabetic subjects with the following:</p> <ul style="list-style-type: none"> * Age > 30 years * A family history of coronary heart disease * Cigarette smoking * Hypertension * Obesity (> 120% desirable weight) * Albuminuria (micro or macro) * Lipids : <ul style="list-style-type: none"> Cholesterol > 200 mg/dl LDL cholesterol > 100 mg/dl HDL cholesterol < 40 mg/dl in men and 50 mg/dl in women Triglycerides > 150 mg/dl <p>Use of aspirin has not been studied in diabetic individuals under the age of 30 years.</p>
<p>3. Use aspirin in doses of 75-325 mg/day.</p>
<p>4. People with aspirin allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding, and clinically active hepatic disease are not candidates for aspirin therapy.</p>
<p>5. Aspirin therapy should not be recommended for patients under the age of 21 years because of the increased risk of Reye's syndrome associated with aspirin use in this population.</p>

MICROVASCULAR COMPLICATIONS

DIABETIC NEPHROPATHY

Diabetic nephropathy is one of the commonest cause of end-stage renal disease (ESRD). This is due to the increasing prevalence of type 2 diabetes, longer lifespan of diabetic patients and improved therapeutic options and the fact that patients with diabetic nephropathy are being accepted for renal replacement therapy. Prevalence of all grades of proteinuria was seen in 19.7% of type 2 diabetics and amongst them, 5.5% had nephropathy. The natural history of diabetic nephropathy progresses from normoalbuminuria, through

a subclinical stage of urinary albumin excretion called microalbuminuria to overt proteinuria and eventually end-stage renal disease (Table 7).

TABLE 7 : Stages of diabetic nephropathy

Stage	Designation	Main Characteristics	GFR	Albumin Excretion	BP	Treatment
I.	Hyperfunction Hypertrophy	Large kidney and glomerular size	150	May be increased	Normal	Strict glycemic control reverses the condition
II.	Normoalbuminuria	Normal UAE	With/without hyperfiltration	Normal (often increased in stress situations)	Normal	Strict glycemic control may reduce hyperfiltration
III.	Incipient	Persistently elevated UAE	130-160	20-200 µg/min	Elevated 3-5% yr	Microalbuminuria stabilized by strict treatment, GFR also stable if HbA _{1c} is reduced. Prevention of progression is possible.
IV.	Overt	Clinical proteinuria	10-130	> 200 µg/min	Hypertension	Poor control leads to greater fall in GFR
V.	Uremia	End stage renal failure	0-10	Decreasing	BP is high due to nephron closure	Progression can be retarded by strict glycemic control, BP control.

Prevalence at Various Stages

- I. Acute renal hypertrophy/hyperfunction: Present at diagnosis
- II. Normoalbuminuria: Most patients in the first 5 years
- III. Incipient nephropathy: Occurs after 5-15 years in <126>35% of patients
- IV. Overt diabetic nephropathy: Usually develops in about 35% of patients after 15-25 yrs
- V. End-stage renal disease: Final outcome, usually after 25-30 years

Significance of Albuminuria

Microalbuminuria is a marker of generalized endothelial dysfunction

In type 2 diabetes mellitus, microalbuminuria, May be non-specific. It is correlated with systolic hypertension. Associated cardiovascular disease. Associated peripheral vascular disease, Coronary artery disease occurs earlier than ESRD. Associated with premature atherosclerosis. Abnormal lipid profile and Pronounced increased mortality. The correction of microalbuminuria in isolation may not affect events appreciably.

Screening for Albuminuria

The methods adopted may be

- 24 hour collection along with measurement of creatinine clearance (mg/24 hours)
- Timed collection ($\mu\text{g}/\text{min}$)
- Spot collection to look for albumin to creatinine ratio ($\mu\text{g}/\text{mg}$ creatinine). Sample should not be taken in the immediate post-exercise period. (Table 8).

TABLE 8 : Definitions of abnormal albumin excretion

Category	24 hour collection (mg/24 h)	Timed collection ($\mu\text{g}/\text{min}$)	Spot collection ($\mu\text{g}/\text{mg}$ creatinine)
Normal	< 30	< 20	< 30
Microalbuminuria	30-300	20-200	30-300
Overt albuminuria	> 300	> 200	> 300

In type 1 DM, screening should begin with puberty and after 5 years duration of diabetes. In type 2 DM, however, screening is recommended at the time of diagnosis and if negative, every year.

Routine urinalysis should be performed annually.

Treatment Options

Modalities of treatment depend on the stage of disease at diagnosis (especially type 1 DM) to prevent onset of nephropathy. Treatment approaches are as outlined in Table 9.

TABLE 9 : Treatment options for diabetic nephropathy

<p>Early Nephropathy</p> <ul style="list-style-type: none"> • Tight Glycemic control • Treatment of systemic and intraglomerular hypertension • Dietary protein restriction • Modification of risk factors - smoking and dyslipidemia
<p>End Stage Renal Disease</p> <ul style="list-style-type: none"> • To provide symptomatic relief, control of hypertension • Renal replacement therapy

Glycemic Control

Intensive glycemic control can significantly reduce the risk of developing microalbuminuria and overt nephropathy. Metformin should not be used if the serum creatinine is more than 1.4 mg/dl in men and 1.5 mg/dl in women. Oral antidiabetic drugs recommended for diabetic nephropathy are gliclazide, glipizide, acarbose, repaglinide and nateglinide. However they should be used with caution.

Hypertension Control

In type 1 diabetes mellitus, hypertension is usually due to the development of nephropathy, while in type 2 diabetes mellitus, hypertension is multifactorial. Both systolic and diastolic hypertension can accelerate the progression of diabetic nephropathy and aggressive treatment of hypertension may markedly retard the rate of fall of GFR. The goal of treatment in adults is to maintain a systolic BP < 130 mm Hg and a diastolic BP < 85 mm Hg. In patients with isolated systolic hypertension and an initial systolic BP > 180 mm Hg, the initial goal is to reduce it to < 160 mm Hg, and in those with systolic BP 160-179 mmHg, to lower it by 20 mm Hg. If tolerated, further reduction may be attempted. Lifestyle modification should play a major role in the treatment which includes cessation of smoking. The drug of choice, as per current evidence, is an angiotensin converting enzyme inhibitor (ACEI) or ARB. This group of drugs has shown benefit in reducing the progression of microalbuminuria in all patients with type 1 DM and in normotensive and hypertensive patients with type 2 DM. In normotensive diabetics with normal renal function in the absence of albuminuria, there is not enough evidence for the use of ACEIs. Use of betablockers and loop diuretics may be considered in the event of the failure of ACEIs and long acting calcium channel blockers. ACEIs should be withheld once the serum creatinine rises above 2 mg/dl or creatinine clearance falls below 30 ml/min. The use of AT₂ receptor blockers are indicated: If ACEIs are not tolerated or It can be added to ACEIs if the BP control is not optimum.

Protein Restriction

Restriction of protein intake can lead to reduction in the hyperfiltration and intraglomerular pressure and thereby retard the progression of nephropathy. (Use of protein derived from soya bean and its products may be preferable). The recommended dietary allowance is 0.8 gm/kg/day. In selected patients with overt nephropathy and falling GFR, a stricter restriction to 0.6 gm/kg/day may be useful.

Other Aspects: Restriction of salt intake to the extent of 4 g/day (to less than 2 g/day in presence of fluid overload). Restriction of phosphate in the diet. Use of calcium containing phosphate binders. Standard treatment for renal disease, as and when indicated, includes, chronic ambulatory peritoneal dialysis, hemodialysis and renal transplantation.

Prevention of Progression of Renal Damage

- Cessation of smoking (any form of tobacco)
- Avoid nephrotoxic drugs
- Prompt treatment of urinary infections and renal stasis
- Caution during contrast study
- Prevention of dehydration
- Use of ACEIs in normotensive diabetics with microalbuminuria retards the progression of microalbuminuria.
- Intensive BP control and control of lipids.

DIABETIC RETINOPATHY

In India, the prevalence of diabetic retinopathy is observed to be 23.7% in a study conducted in South Indian urban population. In an another study, the prevalence was found to be 34.1%. 7.3% has been reported to have retinopathy at diagnosis. Retinopathy contributes to almost 20% of the blindness in the general population. Diabetic retinopathy is asymptomatic until it is advanced. Diabetic blindness is mainly due to maculopathy or proliferative retinopathy. It can also occur due to cataract, glaucoma, and retinal vascular occlusion. The presence of proliferative diabetic retinopathy is an indicator of underlying malignant vasculopathy implying a greater risk of death in such individuals from coronary artery disease, nephropathy and stroke. It is estimated that the risk of death in such patients is seven times higher. Patients with microalbuminuria have 5-10 times greater risk of developing proliferative retinopathy. The main determinant of diabetic retinopathy is the duration of diabetes and quality of glycemic control. Environmental and genetic factors may also play a role (Table 10). Once retinopathy is established, tight glycemic control cannot retard its progression.

Table 10 : Differences in retinopathy between type 1 and type 2 diabetes mellitus

Type 1	Type 2
Very few patients develop retinopathy in first 5 years Don't develop proliferative retinopathy in first 12 years Prevalence rises after 8 years of diabetes mellitus	20% may have changes of retinopathy at onset 10% of these develop proliferative retinopathy The duration of diabetes mellitus, degree of hyperglycemia, dyslipidemia and hypertension are risk factors

Pathophysiology: Retinopathy is due to microvascular disease where there is loss of pericytes and capillary basement membrane thickening which are early signs of abnormalities. Two main pathological processes are capillary occlusion causing ischemia and capillary leakage causing exudation and edema. The ischemia produces angioproliferative factors which produces neovascularization and proliferative retinopathy.

Stages of Diabetic Retinopathy

<p>1. Background</p> <ul style="list-style-type: none"> • Microaneurysms • Scattered exudates • Hard exudates • Hemorrhages <ul style="list-style-type: none"> * Flame shape, * Dot and blot • Cotton wool exudates <ul style="list-style-type: none"> * Spots ≤ 5) • Venous dilatation <p>2. Pre-proliferative</p> <ul style="list-style-type: none"> • Rapid increase in microaneurysm count • Intraretinal microvascular abnormalities • Multiple hemorrhages • Cotton wool spots (> 5) • Venous beading, looping and duplication 	<p>3. Proliferative</p> <ul style="list-style-type: none"> • New vessels <ul style="list-style-type: none"> * On disc (NVD) * Elsewhere (NVE) • Fibrous proliferation <ul style="list-style-type: none"> * On disc (FPD) * Elsewhere (FPE) • Hemorrhages <ul style="list-style-type: none"> * Preretinal, * Vitreous <p>4. Advanced Diabetic Eye Disease</p> <ul style="list-style-type: none"> • Retinal detachment • \pm Retinal tears • Rubeosis iridis • Neovascular glaucoma <p>5. Maculopathy</p> <ul style="list-style-type: none"> • Macular edema <ul style="list-style-type: none"> * Focal, * Diffuse • Ischemic maculopathy
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Treatment

Periodic ophthalmic checkup, Tight glucose control, Tight control of blood pressure, Strict Lipid control, Cessation of smoking

Condition	Recommend Action
NVD	Pan-retinal photocoagulation before vitreous hemorrhage occurs
NVE	Pan-retinal photocoagulation before retinal detachment occurs
Rubeosis iridis	Pan-retinal photocoagulation before neovascular glaucoma develops
Pre-proliferative	Pan-retinal photocoagulation, of one eye initially

Vitreo-retinal surgery for the ultimate blinding complications of proliferative diabetic retinopathy i.e. severe vitreous hemorrhage, secondary retinal detachment and neovascular glaucoma (Table 11).

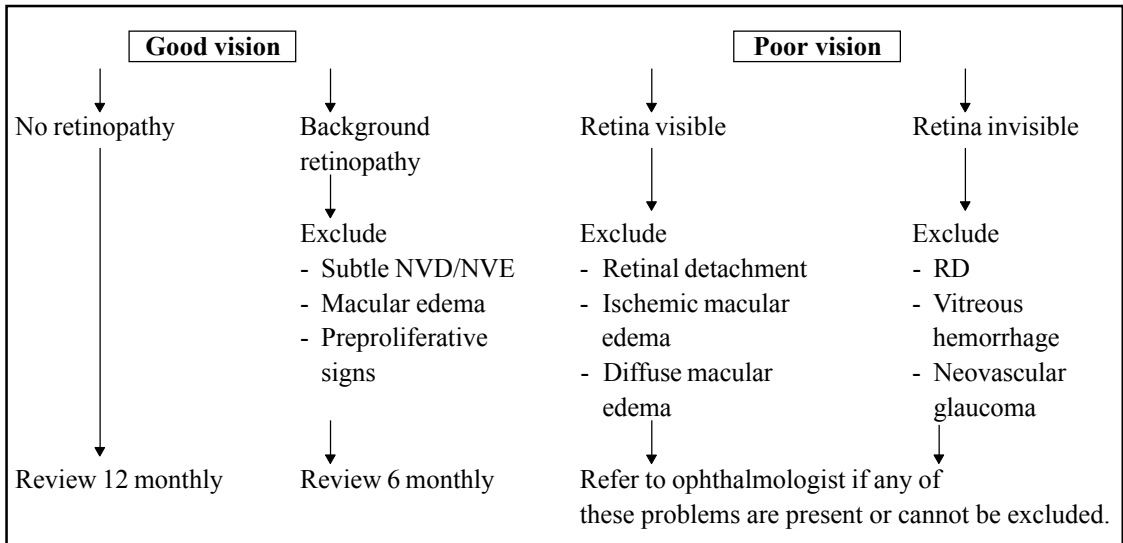
Table 11 : Examination of the Eyes in Diabetic patients

When to examine	What to do
<p>At diagnosis Visual acuity</p> <ul style="list-style-type: none"> - distant vision (Snellen chart) - near vision (reading chart) <p>Annually thereafter</p> <p>Biannually if background retinopathy is present</p> <p>Four-monthly if mild pre-proliferative changes occur</p> <p>Immediately if any change in vision or visual symptoms</p>	<p>Check pupillary light reflexes for relative afferent defect</p> <p>Fundoscopy, through dilated pupils</p> <p>Specialist ophthalmological investigations</p> <p>Slit lamp examination of iris anterior chamber and retina</p> <p>Measurement of intraocular pressure</p>

Causes of Sudden Blindness in Diabetes

- Retinal detachment
- Vitreous hemorrhage and retinal hemorrhage
- Central retinal vein thrombosis
- Arterial occlusion
- Optic neuritis
- Acute glaucoma

Flow Chart for Reviewing Patients with Diabetic Retinopathy



DIABETIC NEUROPATHY

Most common and troublesome complication of diabetes mellitus leading to the greatest morbidity and resulting in huge economic burden for diabetic patients and his family.

Diabetic neuropathy is a heterogenous disorder that encompasses a wide range of abnormalities affecting proximal and distal peripheral sensory and motor nerves as well as the autonomic nervous system.

Clinical Classification

- I. Progressive neuropathies
- II. Reversible neuropathies
- III. Pressure palsies

I. Progressive Neuropathies

<ol style="list-style-type: none"> 1. Distal symmetrical polyneuropathy <ul style="list-style-type: none"> ◆ Predominantly sensory ◆ Autonomic involvement common (mostly asymptomatic) ◆ Clinical motor involvement very rare 	<ol style="list-style-type: none"> 2. Small fibre neuropathy <ul style="list-style-type: none"> ◆ Autonomic involvement common and usually symptomatic ◆ Gradual onset ◆ No recovery ◆ Associated with increasing duration of diabetes ◆ Associated with other chronic diabetic complications
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II. Reversible neuropathy

<ul style="list-style-type: none"> • Mononeuropathies <ul style="list-style-type: none"> ◆ Femoral (amyotrophy) ◆ Cranial nerve palsies (III and VI) ◆ Truncal radiculopathies 	<ul style="list-style-type: none"> • Acute diffuse painful neuropathy <ul style="list-style-type: none"> ◆ Stocking distribution Sudden onset ◆ Spontaneous recovery ◆ No association with duration of Diabetes ◆ No association with other chronic diabetic complications
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III. Entrapment Neuropathies

<ul style="list-style-type: none"> ◆ Median nerve ◆ Ulnar nerve ◆ Lateral popliteal nerve ◆ More common than in the non-diabetic population ◆ No association with duration of diabetes

Clinical Presentation of Large Fiber Neuropathies

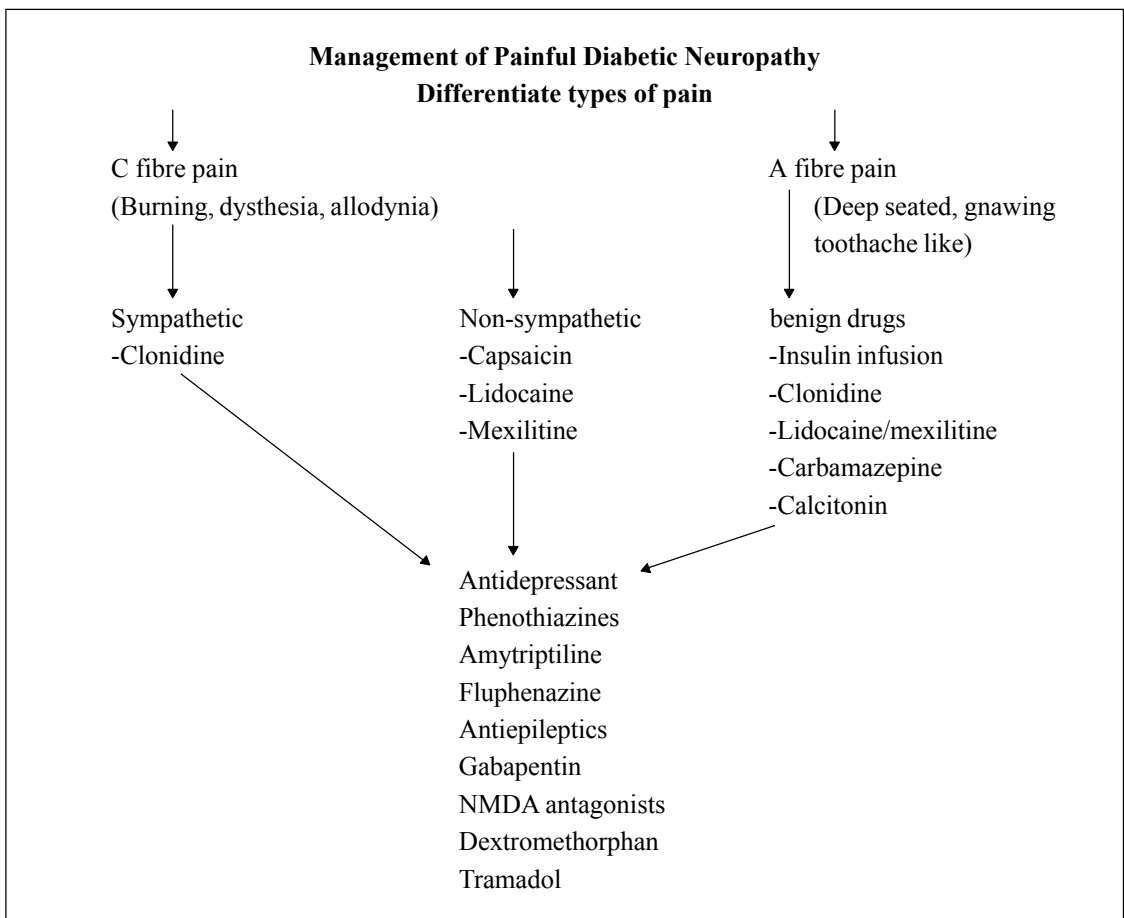
- Impaired vibration perception (often the first objective evidence) and position sense
- Loss of ankle jerk
- Sensory ataxia (waddling gait like a duck)
- Shortening of achilles tendon with pes equinus
- Increased blood flow (hot foot)

Clinical and Subclinical Features of Autonomic Neuropathy

- **Symptomatic** : Gustatory / patchy sweating, postural hypotension, gastroparesis, diabetic diarrhoea, neuropathic bladder, erectile dysfunction, warm dry skin, loss of hair & / venous congestion
- **Subclinical** : Abnormal pupillary reflexes, oesophageal dysfunction, abnormal cardiovascular reflexes & increased peripheral blood flow.

Management of Neuropathy

- Control of hyperglycemia
- Aldose reductase inhibitors (ARIs)
 - ◆ Tolerestat, Zenarestat, Zopolrestat etc.
- Alpha-lipoic acid and methylcobalamin
- Agents still under Investigation Gamma-linolenic acid, Aminoguanidine
- Intravenous human immunoglobulin, Neurotrophic therapy



Management of Autonomic Neuropathy

Postural hypotension

- Supportive garments
- Drug therapy : 9-alpha flurohydrocortisone (possible role)

Gastropathy

- Multiple small feeds
- Mosapride
- Domperidone
- Erythromycin
- Jejunostomy

Cystopathy

- Bethanechol
- Self catheterization

Gustatory sweating

- Topical glycopyrrolate

Management of Erectile Dysfunction

One must exclude other causes of erectile dysfunction such as drugs, androgen deficiency and psychological factors. Sildenafil citrate can be administered if it not contraindicated. Intracavernous papavarine injections have shown benefit. Intractable cases may be referred to the urologist.

Bedside Assessment of Autonomic Neuropathy

- Postural hypotension
- Pupillary light reflex
- Resting tachycardia
- Post-void distended bladder

DIABETIC FOOT SYNDROME

Foot problems such as ulcerations, infections, gangrene and amputations are quite common in diabetic subjects. These account for their frequent and prolonged hospitalization, significant morbidity and even mortality. On a rough estimate nearly 20% of all hospital admissions of diabetes are due to foot problems and nearly 5-10% may need foot/leg amputation. Moreover, of all the non-traumatic amputations approximately 50% are related to diabetes. The economic and psychological stress for the family and the patient are enormous. However with proper foot care these could be prevented or minimized.

Etiopathogenesis of Foot Lesions in Diabetics

Peripheral vascular disease (PVD), neuropathy (peripheral and autonomic) and infection are the three major etiological factors either singly or in combination. In India, infection plays an important part.

Clinical Evaluation Guidelines

- **Ischaemic foot**
 - ◆ History of claudication, rest pain
 - ◆ Palpation of peripheral pulses
 - ◆ Ankle-brachial pressure index (ABR below 0.8 indicates ischaemia)
 - ◆ Doppler ultrasound and other tests
- **Neuropathic foot**
 - ◆ History of nocturnal pain
 - ◆ Skin texture, fissuring, dryness
 - ◆ Semmes Weinstein microfilament test
 - ◆ Vibration test and ankle jerk
 - ◆ Motor power-atrophy
 - ◆ Biothesiometry
 - ◆ Nerve conduction studies

Clinical Spectrum of Diabetic Foot Lesions

- Onychomycosis
- Paronychia
- Infected foot ulcer
- Necrotizing fasciitis
- Osteomyelitis
- Charcot's neuroarthropathy
- Gangrene

Risk Factors for Diabetic Foot Lesion

- Insensitive foot - loss of protective sensation leading to burns or injury
- Altered foot biomechanics - deformed foot
- Increased pressure points - corns, callosities, erythema

- Impaired peripheral circulation - ischemic foot
- Severe nail pathology - ingrowing nails
- Loss of perspiration - dry skin, fissuring
- Limited joint mobility - 'intrinsic minus' foot
- Bare foot walking
- Rat bite
- Edema feet - congestive heart failure, nephropathy
- Past history of foot ulceration, gangrene, amputation
- Epidermophytosis of web space
- Cracks
- Ill-fitting footwear

Wagner's Classification of Foot Lesions

Grade 0 : Foot at high risk - no ulceration

Grade 1 : Superficial ulceration

Grade 2 : Deep ulceration

Grade 3 : Deep ulceration with infection and osteomyelitis

Grade 4 : Forefoot or localized gangrene

Grade 5 : Extensive gangrene requiring amputation

Measures to Improve Vascular Supply

- Control of diabetes, hypertension, dyslipidemia
- Cessation of smoking/tobacco chewing
- Avoidance of
 - ◆ Cold exposure, elastic stocking
 - ◆ Prolonged standing or sitting with crossed legs
 - ◆ Drugs viz. beta-blockers, dopamine, dobutamine
- Control of congestive heart failure
- Supervised graded exercise

Initial Antimicrobial Therapy

Type of lesion	Anti-microbial therapy
Superficial ulcer and non-toxic	Ampicillin+cloxacillin Ampicillin+clavulanate Cephalexin+ciprofloxacin+metronidazole
Deep ulcer and toxic	Ampicillin+cloxacillin+metronidazole Ampicillin+clindamycin Ampicillin+clavulanate Amoxycillin+3rd generation cephalosporin +metronidazole

The choice of antibiotics will ultimately depend on the progression of the foot lesion and culture sensitivity report.

General Management Plan for Infected Foot Lesions

- Immobilization of the extremity, drainage of pus
- Early surgical intervention (if planter mid-compartment is affected)
- Aggressive debridement of necrotic and infected tissue
- Avoid tight bandage in fulminant infection with soft tissue swelling (it prevents pressure necrosis).
- Suspect osteomyelitis in deep lesions especially if bone is felt on probing - confirm by radiography.
- Proper local care of wound, removal of slough and dressing
- Consider use of hyperbaric oxygen therapy wherever indicated.
- Doppler ultrasound to detect vascular pathology

Management of Acute Ischemic Foot

Pentoxifylline, clopidogrel.

Low molecular weight heparin for hemodilution and defibrogenation.

Vascular reconstructive surgery.

Balloon angioplasty.

General Plan of Management

Grade of lesion	Management plan
Grade 0	Strict control of diabetes Prompt treatment of superficial bacterial /fungal infection Tetanus prophylaxis
Grade I	Above + Rest to the limb Avoid weight bearing Ensure adequate drainage Proper surgical care
Grade II and above	Above + Broad spectrum antibiotics Debridement of necrotic tissue Frequent dressing, removal of slough Revascularisation procedures Rarely amputations if chronic non-healing ulcer/gangrene

In India, the neuropathic foot is more common as compared to the ischaemic foot. This diabetic foot can be treated effectively by off loading the body weight by proper foot wear in the grade 0-3 and total contact casting and bed rest in grade 4 along with the use of appropriate antibiotics. These measures can prevent many amputations in neuropathic diabetic foot.

Guidelines for Preventive Measures

- Assess the patient's knowledge and foot care practices.
- Advise essential guidelines for preventive foot care.
- Advise to consult the doctor if swelling of foot, color change of toe/nail, pain or throbbing, thick hard skin or corns, breaks in skin, cracks, blisters or sores.
- Identification of foot at risk (low and high risk) and take measure to prevent foot ulceration in them.
- Assess at each visit for protective sensation (touch, pain and vibration), foot structure, biomechanics, vascular status and skin integrity.
- Evaluation for additional risk factors and plan strategies accordingly.

Foot Care Guidelines for Diabetes

Do's	Dont's
<p>Wash feet daily</p> <p>Inspect feet daily (use mirror)</p> <p>Keep feet dry especially web spaces</p> <p>Use cotton socks without elastic</p> <p>Canvas shoes/sandals with velcro and MC insole should be used.</p> <p>Use broad size well fitting shoes with soft soles, stitched not nailed</p>	<p>Application of hot/cold water</p> <p>Soaking foot in warm water</p> <p>Walking on hot or cold surface/ barefoot walking</p> <p>Tight shoes</p> <p>Self treatment of corn or callus/use of corn caps</p> <p>Delay in seeking the medical advice</p> <p>Do not cut the nail too short and use nail cutter</p>

Footwear Advise for the Diabetic Patient

- Hawaii slippers and strap slippers should not be used.
- Sandals are recommended with velcro.
- Shoes with broad front should be used.
- Shoes must be roomy.
- Use of insoles in early foot lesions.
- Footwear should be ideally purchased in the evening.
- Use custom made shoes for advanced diabetic lesions.

SPECIAL SITUATIONS

INFECTIONS

The relationship between diabetes mellitus and infections is synergistic (Table 12). [Infections account for nearly 10% and 40% of deaths in type 1 and type 2 diabetics respectively. However in developing countries, these infections are relatively more common]

TABLE 12 : Diabetes and infection : A Synergistic combination

<p>Effects of diabetes on infections</p> <ul style="list-style-type: none"> * Defective granulocyte, macrophage and lymphocyte function * Infection is more severe, prolonged and resistant to treatment
<p>Effect of infections on diabetes</p> <ul style="list-style-type: none"> * Worsening hyperglycemia * Precipitation of ketoacidosis

TABLE 13 : Important infections associated with diabetes

<p>Respiratory</p> <ul style="list-style-type: none"> Tuberculosis Mucormycosis <p>Gastrointestinal</p> <ul style="list-style-type: none"> Emphysematous Cholecystitis Candidiasis <p>Urinary tract</p> <ul style="list-style-type: none"> Emphysematous pyelonephritis Upper/Lower urinary tract infection 	<p>Skin</p> <ul style="list-style-type: none"> Dermatophytosis Candidiasis Staphylococcal infections Carbuncles, paronychia <p>Soft tissue</p> <ul style="list-style-type: none"> Necrotizing fasciitis Infected foot ulcer Malignant otitis externa Diabetic hand syndrome <p>Bone</p> <ul style="list-style-type: none"> Osteomyelitis Uncommon infections Fungal meningitis Melioidosis Salmonella enteritis
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Tuberculosis (TB)

Tuberculosis is two to three times more common in diabetics and is an important cause of cachexia in them. 10% of Diabetics have TB and 20% of TB patients have associated

diabetes. The clinical spectrum is characteristically different (Table 13). However, antituberculous therapy can interfere with the glycemetic control. Most patients have cachexia and would require insulin. Occasionally subjects with mild diabetes, early tuberculosis and normal BMI can be managed on oral drugs. However, the requirement of oral drugs increases. Antitubercular therapy is however no different from non-diabetics; a four-drug regimen for 2 months and a two-drug regimen for the next 4 months is usually adequate.

Reactivation of TB occurs if glycemetic control is ineffective. For non-caseous TB, oral drugs can be used whereas for caseous TB, insulin is to be preferred. Monitoring needs to be done more frequently since the requirements of antidiabetic drugs may be high. The diabetes should be controlled intensively and urgently.

TABLE 14 : Characteristics of diabetes-related tuberculosis

- More advanced, Severe
- Lower lobe, bilateral and often nonsegmental
- Increased incidence of lung cavitation and sputum positivity
- Higher rates of relapse and multidrug resistance.
- Predeliction for undernourished and young diabetics.
- Brittle glycaemia

Mucormycosis

Mucor species cause infection in the immunocompromised, acidotic and hyperglycemic states. Rhinocerebral mucormycosis usually presents with facial (periorbital or perinasal) swelling associated with erythema, induration and a bloody discharge. A black necrotic eschar on the nasal turbinate may be an early finding. Later, proptosis, ophthalmoplegia and cranial nerve palsies result. Thrombosis of the cavernous sinus and internal carotid artery may also occur. Tissue biopsy shows characteristic broad, nonseptate, haphazardly branching hyphae. Mortality is about 50%, despite amphotericin B, surgical debridement and hyperbaric oxygen therapy. Pulmonary mucormycosis mimics any chest infection, but the CT scan shows a typical “halo” sign. Amphotericin B is given in increasing doses with a target dose of 1-1.5 mg/kg intravenously daily.

TABLE 15 : The spectrum of diabetes-related candida infection

Infection	Therapy
Oral candidiasis	Topical Imidazoles
Paronychia	Oral Fluconazole
Vulvitis	Imidazole suppositories
Balanitis	Topical Imidazoles
Esophagitis	Fluconazole
Urinary tract infection (cystourethritis)	Bladder irrigation with Amphotericin B/oral Flucytosin (for 4 days)
Invasive/systemic candidiasis	Amphotericin B

Table 16 : Treatment of some diabetes-related infections

Infection	Organism	Drug of initial choice
Community acquired pneumonia (out-patient)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>S. aureus</i> , atypical pathogens	Azithromycin or Doxycycline
Community acquired pneumonia (hospitalized)	Same as above	Ceftriaxone or Cefuroxime (parenteral)
Acute bacterial cystitis	<i>E. coli</i> , <i>Proteus</i> and Gram-negative pathogens	Trimethoprim Sulfamethoxazole
Acute pyelonephritis /perinephric abscess	<i>Staph. aureus</i> + Same as above	Ciprofloxacin, for <i>S. aureus</i> infection: Nafcillin or Cefazolin
Necrotizing fasciitis	Gram-negative bacilli, anaerobes, group A Streptococci	Penicillin G + Clindamycin + Gentamicin
Malignant otitis externa	<i>Pseudomonas aeruginosa</i>	Ciprofloxacin (intravenous)
Emphysematous cholecystitis	Gram-negative bacilli, anaerobes	Ampicillin + Sulbactam

Diabetes and Infection : A Preventable Problem

Infections are a preventable cause of hyperglycemia and ketoacidosis in diabetics. The vicious combination of diabetes and infection can be broken by the judicious use of antimicrobial therapy and glycemetic control. Near-normal glycemetic should be the target in such subjects. Insulin therapy should be instituted, and it is often possible to withdraw insulin and start on oral drugs after the infection has subsided in order to improve patient compliance.

SURGERY

Surgical intervention in diabetic patients require additional care. Surgery and diabetes both adversely affect each other. With careful pre-operative assessment and proper preparation, elective surgery can be performed. Choice of appropriate anesthetic agent to avoid metabolic derangement is recommended. Life-threatening surgical situations can be treated irrespective of blood glucose level with aggressive management of diabetic status. No diabetic should be debarred from the benefit of surgery. Ketoacidosis, osmotic diuresis, electrolyte imbalance and infection alter the surgical outcome.

General anesthesia induces a stress and results in secretion of counter-regulatory hormones raising the blood glucose. Spinal and epidural anaesthesia blocks splanchnic supply leading to fall of plasma catecholamine requiring less insulin and thus there is more chance of hypoglycemia. When anesthesia is over, blood glucose starts rising, due to surgical stress. Halothane and enflurane are safer anesthetic agents. Local anesthetic is considered safe in diabetics.

Minor surgery does not require change of medication if there is good glycemetic control.

Pre-operative Management (For Major Surgery)**Preoperative Assessment for**

- Glycemetic status
- Cardiac evaluation
- Hypertension
- Diabetic nephropathy
- Diabetic neuropathy
- Autonomic neuropathy
- Renal parameters

The glycemetic control is aimed to achieve a fasting plasma glucose of $\ll 126$ mg/dl and a post-prandial glucose of < 200 mg/dl.

- In patients with good control on oral antidiabetic drugs, stop OHAs on the day of surgery and put them on IV fluids and insulin.
- In patients on long acting antidiabetic agents, despite good control, stop the drugs 3 days before surgery and admit the patient for insulin therapy.
- Diabetics who are not under control, are to be admitted for stabilizing with insulin. The insulin therapy should be individualised depending on the blood glucose profile. Use of multiple subcutaneous short acting insulin is advisable for effective glycemic control.

On the Day of the Surgery

- The most effective and reliable method of administration of insulin is the IV route. Subcutaneous route is not recommended.
- It is preferable to take the diabetic patients for surgery in the morning as the first case.
- Insulin glucose infusion should be used and blood glucose should be monitored every hour.
- During surgery, 5% dextrose infusion with appropriate amount of (8-10 units per pint) insulin in the drip or in major surgeries, insulin can be administered by infusion pumps.
- Continuous blood glucose monitoring is recommended.

Monitoring of Blood Glucose

Continuous intra- and postoperative ECG is required in case of patient:

- Above the age of 40 years
- With DKA
- Acid base and/or electrolyte imbalance
- Exposed to hypotension during surgery

CVP measurement is required in:

- Cardiac surgery
- Dehydration
- Renal failure

Monitor urinary output if necessary by catheter in

- Renal failure
- Hypotension during surgery.

Post-operative Management

In uneventful recovery, the patient can be switched to presurgery antidiabetic therapy after total surgical healing (2-4 weeks). Drugs can be started after at least 4 weeks if there are no complications of surgery.

Use of IV Fluids

1. Dextrose saline/normal saline is used if BP is normal or low.
2. In situations needing fluid restriction, 10% dextrose can be infused instead of 5% dextrose with double the dose of insulin.
3. Avoid Ringer's lactate solution.

Minor Surgery

The antidiabetic drugs and insulin are stopped on the day of the surgery. Once the surgery is over, and the patient is permitted to resume oral feeds, the antidiabetic drugs are started with half the dose which the patient was originally taking. On the second post-operative day, full dose of the oral antidiabetic drugs and or insulin are started. Currently, cataract surgery and superficial abscess drainage can be performed if the patient is under good control with oral antidiabetic agent without changing over to insulin.

Conclusion

Diabetic patients who are undergoing planned surgery if properly scrutinized and prepared in terms of all the metabolic factors and organ complications, the extra risk for diabetes during or after surgery is negligible. In uncontrolled severe diabetes, the case should be managed as a case of DKA and prepared within a short period. Diabetes is not a contraindication for surgery.

PREGNANCY AND DIABETES

Diabetes and pregnancy encompasses not only a known diabetic marching through pregnancy but also any form of abnormal glucose tolerance developing during gestation. The abnormal glucose tolerance of any etiology, during pregnancy is associated with the high risk of a poor outcome like miscarriages, stillbirth, neonates with heavy birth weight, small for dates, children with lethal or morbid congenital malformations.

Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy. The definition applies whether insulin or only diet modification is used for treatment and whether or not the condition persists

after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with pregnancy. Risk assessment for GDM should be undertaken at the first prenatal / antenatal visit. Women with clinical characteristics consistent with a high risk of GDM (Table 17) should undergo glucose testing as soon as feasible. If they are found not to have GDM at that initial screening, they should be retested between 24 and 28 weeks of gestation. Women of average risk should have testing undertaken at 24-28 weeks of gestation. Low risk status requires no glucose testing, but this category is limited to those women meeting the characteristics as given in Table 18.

TABLE 17 : Indications for screening

- Age > 25 years
- Family history of diabetes
- Obesity (pre-pregnancy BMI > 25)
- Bad obstetric history - previous history of
 - ◆ Unexplained perinatal loss
 - ◆ IUD
 - ◆ Large for gestational age infant
 - ◆ Congenitally malformed infant
 - ◆ Polyhydroamnios
 - ◆ Pre-eclampsia
- <195> Glucose in second fasting urine sample

Screening and Diagnosis

Urine Glucose: No Role

Glucosuria is a commonly employed screening test for the detection of glucose intolerance. During pregnancy, the renal threshold for glucose is often lowered, due partly to an eight-fold increase in glomerular filtration of glucose, and partly, to an intermittent tubular defect in glucose reabsorption. Low renal threshold for glucose during pregnancy renders glucosuria less specific for detection of GDM and **must not be used as a diagnostic test**.

TABLE 18 : Low-risk states where screening is not required

- Age < 25 years
- Weight normal before pregnancy
- No known diabetes in first degree relatives
- No history of abnormal glucose tolerance
- No history of poor obstetric outcome

Blood Glucose

Spot Test : The simplest practical screening procedures, which can be followed is the “Spot Test” based on the study in Madras by Seshiah *et al.* In their study the ± 2 SD figure of the spot test blood glucose (corrected to nearest 5 mg) was 85 mg/dl fasting and 105 mg/dl non-fasting. The approximate plasma glucose values will be around 90 mg/dl and 120 mg/dl, respectively. In pregnant women the fasting and non-fasting glucose never exceeded the above figures. Hence any pregnant woman whose plasma glucose value exceeds these cut-off points should be subjected to an oral glucose tolerance test.

O’Sullivan’s Screening Test : The screening test recommended by O’Sullivan and Mahan is to do blood glucose determination one hour after a 50 g oral glucose load, if plasma glucose is more than 140 mg/dl an oral GTT is ordered. It requires 50 g of glucose and the subject has to remain for an additional one hour in the clinic.

American Diabetes Association (ADA) Criteria : The American Diabetes Association in its position statement 2003, recommends Carpenter and Coustan criteria using 100 gm OGTT. Alternatively, ADA also recommends that, the diagnosis can be made using a 75 gm glucose load and the glucose threshold values are listed for fasting, 1 hour and 2 hours (Table 19); however, this test is not well validated for the detection of at risk infants or mothers as the 100 gm OGTT. If any two of the values meet or exceed the cut-off levels the test is positive for GDM. If the test is negative it is repeated during the subsequent trimester, particularly in those who gain excess weight or shown by clinical examination or ultrasound evidence of macrosomia.

TABLE 19 : Current criteria for diagnosis of GDM using glucose load (plasma values)

	100 g		75 g	
	mg/dl	mmol/L	mg/dl	mmol/L
Fasting	95	5.3	95	5.3
1 hour	180	10.0	180	10.0
2 hour	155	8.6	155	8.6
3 hour	140	7.8		

WHO Criteria : A standard OGTT should be performed after overnight fasting by giving 75 gm of glucose. Plasma glucose is measured at fasting and after 2 hours. Pregnant women who meet WHO criteria for IGT and diabetes are classified as having gestational diabetes mellitus (GDM) (Table 19a).

Table 19a : WHO criteria (plasma glucose)

	FPG (mg/dl)	2h PG (mg/dl)
IGT	< 126	140-200
Diabetes	> 126	>> 200

Glycosylated Hemoglobin (GHb) : GHb is not suitable for screening for gestational diabetes, since it yields false positive results in 41% and false negative in 26%. GHb estimation is useful in pre-gestational diabetes to know the retrospective blood glucose control at the time of conception if performed in the early first trimester. GHb is also useful in monitoring the control during pregnancy but not for day-to-day management.

Serum Fructosamine : Like GHb, serum fructosamine is not a useful screening test for gestational diabetes. This test is useful to assess the short-term state of maternal glucose control during the past two weeks.

Recommendations

As per WHO criteria, FPG < 126 mg/dl is normal, whereas by ADA criteria FPG < 95 mg/dl is normal. The 2 hour post plasma glucose of > 140 mg/dl by WHO criteria and > 155 mg/dl by ADA criteria are abnormal. With the effective treatment available, the WHO criteria of 2 hour PPG > 140 mg/dl and ADA criteria of FPG > 95 mg by identifying a large number of cases have greater potential for prevention of fetal morbidity. Hence, we can adopt FPG > 95 and 2 hour PPG > 140 as diagnostic criteria for GDM.

GTT with 75 gm glucose

	ADA	WHO
FPG	> 95	< 126
2 hour PPG	> 155	> 140

If any one of the criteria is fulfilled i.e., fasting or 2 hr more than the recommended values, the pregnant woman should be considered as having IABG (isolated abnormal blood glucose) and followed similar to GDM.

If the screene has fasting plasma glucose more than 126 mgs and 2 hr post-glucose more than 200 mgs, probably she has been having undetected diabetes prior to conception (pregestational diabetes) which can be confirmed by glycosylated haemoglobin.

The above suggested criteria is only for the diagnosis of GDM. For treatment of glucose intolerance during pregnancy the effort should be to maintain fasting 90 ± 5 mgs and 2 hr

post-meal of 120 ± 5 mgs, so that a mean blood glucose around 105 mgs/dl is maintained as this assures best fetal outcome.

The purpose of intervention in GDM is

1. To reduce neonatal complications like hypoglycemia, hypocalcemia, respiratory distress syndrome, hyperbilirubinemia, polycythemia, intrauterine death etc.
2. To reduce macrosomia
3. To reduce the risk to the mother

Management and Monitoring

The meal plan should allow for appropriate maternal weight gain during pregnancy. Better control is achieved by concentrating on the post-prandial values and not allowing them to exceed 120 mg/dl at 2 hour post-meal. It is practical to check the 2 hour post-breakfast and 2 hour post-lunch glucose levels. Values exceeding 120 mgs/dl require insulin for control. Frequency of monitoring should be twice a week during the initial stage, this is because some patients have severe insulin resistance and may require fairly large doses to achieve control. Once control is established the monitoring can be done every 2 weeks during the second trimester and weekly during the third trimester.

Diet

In addition to calculated calories as per the IBW during pregnancy extra caloric requirement is 150, 300 and 450 calories in the first, second and third trimesters, respectively. This requirement can be met with by adding a cup of milk (150 cal) which would provide protein and even calcium.

Insulin

It is mandatory for the mother to learn self injection. Single injection of intermediate acting insulin given in the morning may be sufficient in some cases. When the requirement goes up, multiple short acting injections will be required to control the blood glucose. Split mixed doses of insulin can also be used. In GDM, in whom insulin is used for the first time it is preferable to choose human insulin. Insulin should be stopped on the day of delivery or caesarean section due to risk of hypoglycemia. Insulin analogues are not recommended during pregnancy based on the present day information.

Oral Antidiabetic Agents

Agents other than insulin are not advisable. Yet there are many patients who present during pregnancy with good control on sulphonylureas. These patients must be switched to insulin and the risk of congenital abnormalities should be assessed by ultrasonography especially after 14 weeks.

Delivery

GDM alone is not an indication for caesarean section unless there is macrosomia with probable cephalopelvic disproportion. In Indian settings induction of labor at 38th week is reasonable. After delivery all infants should be checked for hypoglycemia and hypocalcemia and if necessary given glucose intravenously.

Postpartum

GDM patients should undergo a standard 2 hour OGTT with 75 g of glucose 6 weeks and then 6 months after delivery and thereafter every year. Metaanalysis of available data showed that there is a 40% risk of developing type 2 diabetes at 15 years. The most important predictors for developing type 2 diabetes are a high BMI, the severity of diabetes during pregnancy, early onset during gestation and IGT in the postpartum. There is a small but significant risk of macrovascular disease in these woman; approximately 8% by the age of 60 years.

Pregnancy in Patients with Preexisting Diabetes Mellitus

Preconception counselling is essential for all diabetic women contemplating pregnancy. Diabetics who become pregnant will have a risk of teratogenicity if the glycemic control is poor during the first 12 weeks of gestation. Hence they should be advised to achieve tight control before conception. During the preconception visit, renal function and the eyes should be checked. Those with established renal disease i.e. proteinuria > 1 g/24 hrs and creatinine clearance < 70 ml/min and those with proliferative diabetic retinopathy may be discouraged from attempting pregnancy because there is a risk of accelerated progression of retinopathy and nephropathy.

The patients should be converted to or stabilized on animal/human insulin if on OHA. The fasting and 2 hr post-meal values should be below 95 and 120 mg/dl, respectively. In pregnant diabetics, there is a fall in insulin requirements in the first trimester and then a gradual rise in the second and the third trimester. Thus frequent modification in the dose of insulin is essential. If a patient gets repeated episodes of hypoglycemia, it indicates fetal distress. SMBG must be done at least daily during pregnancy.

Once pregnancy occurs the eyes should be checked every 3 months. In the post-partum period renal status should be reevaluated. There is a risk of pregnancy induced hypertension and the blood pressure should be regularly monitored. Control may be achieved with any suitable combination of short and intermediate acting insulin. The targets are : fasting and pre-meal value of 90 ± 5 mgs/dl; a 2 hr post-meal value of 120 ± 5 mg/dl or less.

Management of Diabetics in the Post-partum Period

- Insulin is indicated since oral drugs are secreted in the milk.
- Progesterone containing oral contraceptives should be avoided.
- Copper containing IUCD should be avoided due to chances of infection.
- It is preferable for a diabetic mother to complete the family and go for sterilization.

TRAVEL DAYS

Diabetics deserve to enjoy their travel as much as non-diabetics. All that it needs is, some advance planning and application of common sense. The need for modified recommendations in Indian circumstances arises on following counts:

1. Wide variation in availability of different food items in different parts of the country.
2. Poor hygienic standards of food and water served in roadside hotels and restaurants.
3. Wide variation in temperature in different parts of the country.
4. Scanty medical facility available in many of the tourist spots in the country.

Considering these factors following guidelines can be recommended.

1. All efforts should be made to achieve a good metabolic control before the proposed journey. This may not be possible if the journey has to be undertaken at short notice. In such situations the person must seek advise from his or her physician and proceed accordingly.
2. Adequate supply of medicines (OHA/insulin), syringes, needles and alcohol swabs should be ensured.

To obviate the eventuality of running out of supply, in case the travel is unexpectedly prolonged, a prescription must be obtained from the treating physician. Generic names of the drugs must be mentioned to avoid confusion on account of wide variability in the brand names.

Availability of a prescription is also helpful in case the person is ever questioned about the syringes, needle, medications and other items carried in relation to treatment and monitoring of diabetes.

3. In case of international travel, the following precautions are desirable.
 - a. One must obtain medical insurance to meet needs of unexpected emergencies.
 - b. It is quite helpful to obtain a list and address of the international diabetes federation organizations. Most countries have such organizations. In case of emergency they can co-ordinate with local physicians or hospitals.

- c. If the person is travelling across the time zone, it is important to learn about scheduling insulin injections and meals.
- d. One must learn reasonably, if not thoroughly about meal exchanges because desired type of food stuffs may not be available everywhere.
- e. If the patient is travelling by air, it is possible to obtain the required meal on advance requisition. Even if this is not possible, correct food can be picked from the meal which is served.

All diabetics should carry an identification tag either in the form of a card, chain or bracelet while travelling.

The travel bag containing medications and prescriptions should not be put in the luggage compartment of a car, bus, train or an aeroplane.

Management of Hypoglycemia

Glucose powder, sugar cubes, must be kept in the bag. It is always advisable to carry some slow acting carbohydrate and protein foods, such as biscuits, cheese, milk, sweets, fresh fruits, etc. This is important, as unexpected delays in meal schedules can occur during travel.

Amongst drinks and beverages, coffee, tea, sugar-free soft drinks, bottled or boiled and chilled water are usually safe.

Prolonged driving should be avoided by the diabetics. At 2-3 hrs intervals some snacks containing slow acting carbohydrates should be consumed. At slightest suggestion of a hypoglycemic reaction, the vehicle should be pulled over to the side of the road and some fast acting food mentioned earlier should be taken. Driving should be resumed 10-15 minutes after the person feels completely comfortable. Diabetics with history of hypoglycemia unawareness should not drive.

Exercise

During journey one must walk at every possible opportunity, be it through the aisle of the train or aeroplane or at various stopovers. Daily routine of exercise must be continued either indoor and outdoor.

Monitoring

Monitoring both for blood glucose and urine ketones should not be forgotten. Frequent monitoring should help in minor adjustment of insulin or OHA dosage if the person has been engaged in fasting or feasting or taking activities which are strenuous.

SICK DAY RULES

Patients generally tend to omit their medications during intercurrent illnesses. This is extremely dangerous because the stress is almost always associated with increased secretion of counter-regulatory hormones leading to a rise in blood glucose in spite of a reduced intake of carbohydrates. Simultaneously increased production of ketoacids might contribute to the metabolic disturbance converting a trivial illness into a hyperglycemic emergency. Therefore it is important to take following precaution during sick days.

1. *Medications* : Insulin should not be omitted just because the person is sick. However dose adjustments must be done depending upon frequent monitoring of blood sugar and urinary ketones.
2. If the person is unable to consume food, then adequate hydration must be ensured through nasogastric tubes or intravenous routes. In all other situations the patient should be encouraged to take adequate amount of fluids, particularly containing salt, glucose and potassium. If the usual meal plans are followed, then sugar-free fluids are recommended. Fruit juices are good in such situations. However if usual meal plans are not followed, then the fluid should contain glucose, e.g., fruit juices, sweetened carbonated beverages like cola, lemonade, coconut water etc.
3. The intercurrent illness, howsoever trivial it may be, should be promptly diagnosed and aggressively treated. The importance of bed rest, antipyretics, antibiotics etc. cannot be overemphasized.

Fasting Days

- Fasting and feasting is better avoided.
- It is preferable to advise not to fast particularly if the diabetes is uncontrolled.
- In case of intermittent fasts, one can omit medication on the day of the fast.
- During fasting, preferred diet should be fruits and vegetables.
- In case the diabetes is controlled, modification in the dosage and timing of drugs should be advised.
- In Ramzan fasting, it is preferable to use the drugs when the fast is broken
- Oral drugs with less chances of hypoglycemia should be preferred.

TYPE 2 DIABETES IN THE YOUNG

While type 2 diabetes is usually seen in the adults, it is also observed in the young. There is an increasing rise in the incidence and this rising incidence is also observed in other countries. The contributing factor is the advent of westernization which has made drastic changes in the lifestyle of children leading to physical inactivity, unhealthy food habits and obesity amongst them. In India about 38% of type 2 diabetes is diagnosed below the age of 40 years and in about 4.8% the diagnosis is made below 25 years of age. The two common non-autoimmune forms of diabetes encountered in the young are: the early onset type 2 diabetes and the maturity onset diabetes of the young (MODY)

Early Onset Type 2 Diabetes Mellitus: The Characteristics are positive Family history, Obesity, High plasma glucose values, Absence of ketoacidosis, They respond to lifestyle modification and oral hypoglycemic agents. It can occur as early as the age of puberty. C peptide values need to be estimated to differentiate it from type 1 diabetes

Malnutrition modulated diabetes mellitus (MMDM) and fibrocalculus pancreatic diabetes (FCPD) have also been described in this age group.

FCPD has a definite marker, whereas MMDM does not have a specific marker.

Patients with MMDM are lean and have a low BMI and require high doses of insulin to achieve normoglycemia and are resistant to ketosis.

Maturity Onset Diabetes of the Young (MODY)

There is an another subset of patients who have a strong family history of diabetes running into three generations and onset below 25 yrs of age who are generally asymptomatic and do not develop ketosis. Their BMI is generally normal and they respond to oral drugs.

Management of Type 2 Diabetes in the Young

Therapy can be initiated with insulin and then reevaluated based on the C peptide levels. Those patients with normal C peptide levels can be treated with OHAs. Special precautions need to be taken because the disease starts early and duration may be long.

DIABETES AND HYPERTENSION

Coexistence of hypertension and diabetes is being increasingly recognized. 30-35% of hypertensives are detected to have diabetes. The prevalence of hypertension is 1.5 to 2 times greater in patients with diabetes mellitus compared with matched non-diabetic individuals. More than 40% of diabetics are hypertensive at diagnosis.

Coexistence of diabetes and hypertension increases the risk of macro- and microvascular disease.

Blood pressure should be measured in the supine, sitting and standing position in a diabetes patient to detect evidence of autonomic neuropathy.

UKPDS has stressed the importance of effective blood pressure control irrespective of the antihypertensive agent used. Lowering blood pressure to a mean of 144/82 mmHg statistically reduced strokes, diabetes related deaths, heart failure, microvascular complications and visual loss. The study also shows that polypharmacy i.e. use of two or more drugs is required for optimal control. The HOT study in diabetic patients has shown significantly lower risk of cardiovascular disease in those patients assigned to the lowest target blood pressure (< 130/85 mmHg)

In the management of diabetic hypertensives, lifestyle modifications have to be more aggressive.

Pharmacological treatment of hypertension in diabetic patients differs due to the effects of certain drugs on the lipid profile, insulin sensitivity and glucose metabolism.

ACE inhibitors have been shown to slow the rate of decline in renal function in diabetic patients. The recently reported Heart Outcomes Prevention Evaluation Study (HOPE) emphasised its importance to reduce the risk of complications of diabetes. ACE inhibitors are recommended as first line drugs for management of a diabetic hypertensive.

Therapy with ACEIs, should not be initiated in patients with serum creatinine > 3 mg/dl and serum K⁺ > 5 mEq/L.

When a patient is on ACEIs, follow up is required and close watch should be done on the above parameters. If a rising trend is seen, therapy should be withdrawn.

ACEIs are contraindicated in bilateral renal artery stenosis and pregnancy.

Long acting calcium channel blockers should be used wherever ACEIs are contraindicated.

Low dose thiazide diuretics are recommended in mild hypertension and in combination with other antihypertensive agents. Frusemide is recommended in patients with fluid overload and end-stage renal disease.

Indapamide is metabolically neutral and can be used in mild hypertension with diabetes.

Beta-blockers potentially mask hypoglycemic symptoms, however at present selective beta blockers are not a major contraindication. Further, there is clear evidence of benefits of beta blockers without intrinsic sympathomimetic activity in diabetic patients after myocardial infarction.

Tight metabolic control of diabetes, effective blood pressure control and low protein diet improves overall outcome.

DIABETES AND HYPERLIPIDEMIA

In type 2 diabetes classical triad of elevated triglyceride, LDL cholesterol and suppressed HDL is seen. The level and metabolism of plasma lipoproteins (Lp) in patients with diabetes mellitus depends on several factors as well as the type of diabetes mellitus. The degree of dyslipidemia is more widespread (Table 20). Several studies have shown that serum Tg and serum cholesterol values were raised in newly diagnosed type 2 diabetics and long term diabetics with fair to poor glycemic control. These abnormalities tended to recover with therapy (non-pharmacological and pharmacological) and improved glycemic control. The goals to be achieved in patients with hyperlipidemia are as given in Table 21.

TABLE 20 : Lipid and lipoprotein abnormalities in type 2 diabetes mellitus

LDL-c (including small dense LDL)	Normal or raised
HDL-c	Low or normal
Triglycerides	Usually increased
Total cholesterol	May be increased or normal

TABLE 21 : Lipids and lipoprotein cholesterol levels desirable in patients with diabetes mellitus in India (in mg/dl)

	LDL-c	Triglyceride	Total chol	HDL-c
Diabetes without vascular complication	< 100	< 150	< 200	> 45
Diabetes with vascular complication	< 100	< 120	< 180	> 45

Management

Management of hyperlipidemia in diabetics shares many factors in common with non-diabetics yet the following points have to be given due attention.

1. Sustained control of glycemic states and maintenance of normoglycemia usually corrects diabetes induced hyperlipidemia.
2. Lifestyle modification i.e. diet, exercise, cessation of smoking and alcohol is an integral part of diabetes management and should favorably influence the lipid profile.
3. If total serum cholesterol or LDL-c is raised, then statins are the drug of choice.
4. Raised Tg levels are first managed by good glycemic control.
5. Reduced HDL levels can be raised with the help of exercise.

6. Bile acid sequestrants to be avoided in patients with fibrocalculus pancreatic diabetes as it can worsen malabsorption.
7. Omega-3 fatty acids (fish oil) can be used since it enhances fluidity of cell membrane and reduces insulin resistance.
8. Fibric acid derivatives especially bezafibrate and fenofibrate are advantageous as they help to increase insulin-sensitivity.

TABLE 22 : Step-care approach to management of dyslipidemia in type 2 diabetes

Step I	Non-pharmacological measures Diet therapy Energy restriction Composition Physical activity
Step II	Hypoglycemic drugs Sulfonylurea Biguanides Glitazones Insulin
Step III	Lipid lowering drugs Statins Bile acid sequestrants Fibrates Nicotinic acid Probucol Estrogens

TABLE 23 : Choice of lipid lowering agents

LDL-c lowering	Statins Fenofibrate
HDL-c raising	Nicotinic acid or fibrates
Triglycerides lowering	Fibrates
Combined dyslipidemia	Statins (high dose) Statins + fibrates Statins + nicotinic acid (check blood glucose levels)

HOSPITALISATION

Inpatient care or hospitalization may be appropriate in the following situations:

- Life threatening acute metabolic complications of diabetes like DKA, HONK, hypoglycemia with neuroglycopenia and lactic acidosis.
- Substantial and chronic poor metabolic control that necessitates close monitoring of the patient to determine the etiology of uncontrolled hyperglycemia, with the subsequent modification of therapy.
 - Hyperglycemia associated with volume depletion
 - Persistent refractory hyperglycemia associated with metabolic deterioration.
 - Recurring episodes of severe hypoglycemia (i.e. < 50 mg/dl) despite intervention.
 - Instability manifested by frequent swings between hypoglycemia (< 50 mg/dl) and fasting hyperglycemia (> 300 mg/dl)
- Severe chronic complications of diabetes that require intensive treatment or other severe conditions unrelated to diabetes that significantly affect its control or are complicated by diabetes.
- Diabetic foot
- Other acute medical emergencies

Admission for Complications of Diabetes or for Other Acute Medical Emergencies

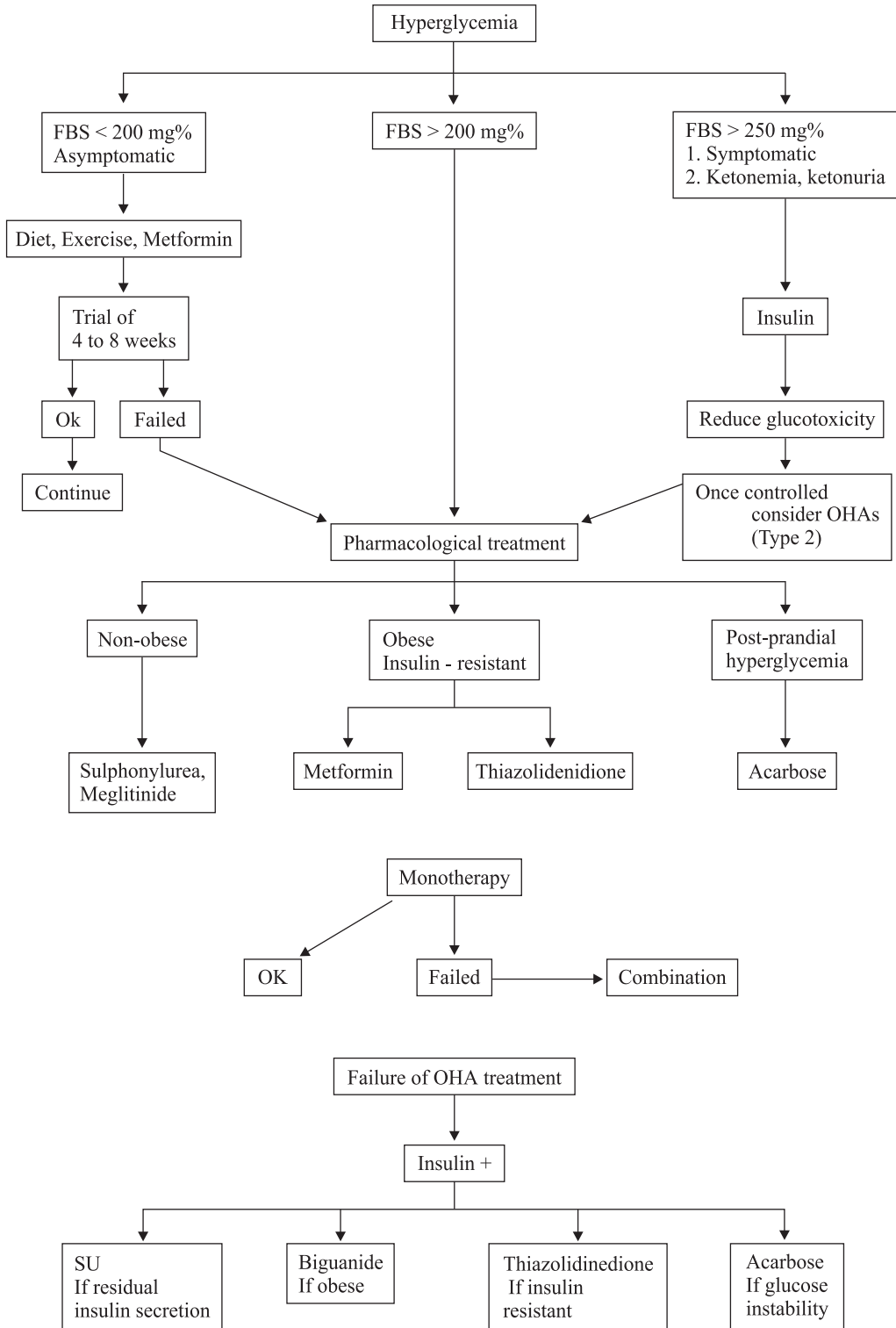
Chronic cardiovascular, neurological, renal and other diabetic complications may progress to the stage where hospital admission is appropriate.

In these situations, the need governing admission for the complication per se (e.g. management of end-stage renal disease) are the primary guidelines for determining whether inpatient care is required.

However, in applying such guidelines, the fact that diabetes is present must be considered; this may result in patients requiring admission who otherwise might be managed on an outpatient basis.

The same is true for other medical conditions (e.g. infarctions) and treatments (e.g. surgery, chemotherapy) in which

1. Diabetes is a confounding factor,
2. Rapid initiation of rigorous control of diabetes can improve outcome (e.g. pregnancy),
3. The primary medical problem or the therapeutic intervention (e.g. large doses of glucocorticoid) can cause a major deterioration in diabetes control, or
4. There is acute onset of retinal, renal, neurological, or cardiovascular complications of diabetes.



Algorithm for the management of type 2 diabetes mellitus