

MANAGING DIABETES MELLITUS

Guide for Health Workers



**ROYAL GOVERNMENT OF BHUTAN
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Author:

Dr. Bhakta Raj Giri MD. Senior Medical Specialist
Dr. Karma Tobgyel MD. Maxillofacial Surgeon
Maj. (Dr.) Hari Chhetri MD. Paediatrician

Review Committee Members:

Dr. Ballab Sharma MD. Senior Medical Specialist
Dr. Tobgay Wangchuck MD. Medical Superintendent
Dr. Tandin Dorji MD, MPH. Paediatrician
Maj (Dr.) D.B. Subba MD. Senior Medical Specialist
Lt.Col. (Dr) T.B. Rai MD. Senior Medical Specialist
Mr. Rup Narayan Chapagai, Chief Programme Officer, DMS
Mr. Yeshi Wangdi, Programme Officer, DMS
Mr. Chador Wangdi, Assistant Programme Officer, DMS
Dr. Ngawang Tenzin, Medical Director, JDWNRH

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Foreword

Diabetes is a chronic, degenerative and life long disorder. WHO estimated a global prevalence of diabetes of 194 millions for 2003 and it is estimated that by 2025 there will be 333 million people living with diabetes world wide. Diabetes is more prevalent in urban settings than in rural. Its prevalence in cities in neighboring countries ranges between 11% - 14% of the population. This rapid increase is due to increased life expectancy, sedentary life styles and changing dietary habits.

The Royal Government's social spending has always remained very high throughout the planned period. Over 24% of total allocations during the current five year plan (2002-2007) have been allocated to health and education sectors. This is so, because Bhutan's unique development philosophy of Gross national Happiness (GNH) like the human development concept of United Nations, places well being of its people at the center of development.

Recognizing diabetes as a serious non communicable disease the Ministry in collaboration with World Diabetes Foundation (WDF) since July, 2005 is publishing guide for Health Workers on Managing Diabetes with objectives of tackling diabetes, an emerging disease that has inflicted the Bhutanese populations but the extent of which yet to be ascertained.

This guide is designed to provide information on managing diabetes mellitus and its complications for all categories of health workers. And this will be made available at all hospitals and health centers for every day use.

I fervently hope that the health workers use this manual at every opportunity in educating people on preventing diabetes to those who are at risk of developing the disease, managing diabetes optimally in those who already have the disease so that they can lead the best possible life.

I am pleased that task force members have shown great interest and worked hard in bringing out the guide. I would also like to acknowledge the financial support of World Diabetes Foundation (WDF) and technical input of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder (BIRDEM) in preparing this very important guide.



Dr. Jigmi Singay
Minister
Ministry of Health

Preface

Diabetes is one important and fast increasing non communicable diseases of the developing world. The prevalence of this disorder is yet to be ascertained but estimates have been made of 2.1 to 2.3 percent of Bhutanese population to be living with diabetes. Prevalence of this disorder is already much higher in the neighboring countries.

Diabetes is a life long disorder. A diabetic can lead a normal life if the condition is detected early and it is managed adequately. However, inadequate or 'non-management' is fraught with several life threatening acute and debilitating chronic complications. Costs in managing these chronic complications are enormous.

The most rational approach to managing this disorder is by educating the people of the risk factors of diabetes and diminishing exposure to these risk factors through life style modifications and healthy eating thereby preventing or delaying occurrence of the disorder. It is equally important to detect the disorder early and institute proper management. Sustained glycemic and blood pressure control prevents end organ damage which can be achieved through a combination of pharmacological and non-pharmacological means.

A diabetic must understand the disease and actively participate in its management. The family members must be supportive and help the diabetic in his/her life style and dietary modification measures. A diabetic must follow up with his/her health worker, get periodic assessment and receive medications that are tailored to his/her need. It is pertinent that the health workers fully understand the disorder and assist the diabetic in the management of the disease.

This manual 'Managing Diabetes Mellitus, Guide for Health Workers' aims at presenting a comprehensive knowledge on diabetes, aetiopathology, complications, both acute and chronic, pharmacological management, diet and physical activity, diabetes and surgery, hypertension in diabetes, diabetes in pregnancy, childhood and elderly, dental care in diabetes and preventing diabetes. The manual is intended for day to day use by Doctors, Assistant Clinical Officers, Health Assistants and Nurses at all level of health facilities in Bhutan. It is kept as simple, handy and readable as possible. It is hoped that all health workers use this manual in guiding and managing people living with diabetes.

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Chapter 1

Definition, Diagnosis and Classification of Diabetes Mellitus

Definition, Diagnosis and Classification of Diabetes Mellitus

Dr. B.R. Giri MD.

Diabetes mellitus is a metabolic disorder that result in hyperglycemia due to defects in insulin secretion, insulin action, or both.

Chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organ systems of body, especially the eye, kidney, heart, blood vessel and the nerves.

Hyperglycemia is either due to lack of insulin or to an excess of factors which oppose its action.

This imbalance leads to abnormalities of carbohydrate, protein and lipid metabolism.

Table 1.1

Plasma glucose cutoffs for diabetes and impaired glucose tolerance

	Fasting plasma glucose (mg/dl)	2 hours post 75 grams glucose load (mg/dl)	Plasma glucose cutoff as risk factor for the following
Diabetes	≥ 126	≥ 200	Eye, Kidney, Nerve and Cardiovascular diseases
IGT	≤ 126	140-199	Diabetes and Cardiovascular diseases
IFG	111-126	Not Applicable	Not well studied
GDM	111-126	>140	

IGT: Impaired Glucose Tolerance, IFG: Impaired Fasting Glucose, GDM: Gestational Diabetes Mellitus

1.1. Aetiopathogenesis

Diabetes mellitus results from defects in insulin secretion, insulin action, or both.

Several pathological processes are involved in the causation of diabetes.

1.1.1. Autoimmune Beta cell destruction of pancreas

In Type 1 diabetes there is absolute deficiency of insulin. Individuals at risk to develop Type 1 diabetes have serological markers for autoimmune pathological process occurring in Islets of Langerhans in the pancreas.

Most obvious histological findings of pancreas that had Type 1 Diabetes for a long time is an almost total lack of insulin secreting beta cell, although A and D cells are well preserved. In recent onset Type 1 Diabetes, most islets are insulin deficient. Some islets with residual beta cells show infiltration with chronic inflammatory cells suggesting Insulinitis.

Individuals at risk of Type 1 Diabetes can often be identified by the serological evidence of an autoimmune process occurring in pancreatic islets of Langerhans and by genetic markers.

1.1. 2. Abnormalities of insulin resistance

Insulin resistance is the main mechanism in Type 2 Diabetes where, insulin is generally available in adequate amounts but however, the action of insulin is blunted and hence, resultant hyperglycemia. It is of equal importance that inadequate compensatory insulin secretory response occur due to pancreatic beta cell exhaustion. In this type of diabetes, a degree of hyperglycemia sufficient to cause pathologic and functional changes in various target tissues, but without clinical symptoms may be present for a long duration before diabetes is detected.

1.2. Clinical staging of Diabetes Mellitus and other categories of abnormal glucose tolerance

1. 2.1. Normoglycemia

Individuals with fasting plasma glucose less than 110mg/dl are termed normoglycemic.

1.2.2. Impaired Glucose Tolerance (IGT and IFT)

These represent intermediate state between nondiabetic and diabetic states. These indicate glucose regulation abnormalities, in the fasting and post-meal states. Individual will not have any clinical manifestation. However, macrovascular changes continue to occur in these stages.

1.2.3. Diabetes Mellitus

- Insulin requiring for survival: Type 1 Diabetes Mellitus
- Insulin requiring for optimal control: Type 2 Diabetes Mellitus
- Insulin non-requiring: Adequate control achieved with diet, physical activity and drugs: Type 2 Diabetes Mellitus

1.3. Etiological Classification of Diabetes Mellitus

1.3.1. Type 1 Diabetes Mellitus

There is absolute deficiency of insulin due to rapid and progressive destruction of beta cells in pancreas. The destructive process is generally autoimmune, characterized by presence of autoantibodies against islet cells, GAD or insulin.

The rate of destruction is rapid generally and is most commonly seen in children and young adults. There is a genetic predisposition to autoimmune destruction of beta cells. Some of these patients have other concomitant autoimmune disorder like Grave's disease, Hashimoto's thyroiditis or pernicious anemia.

Type 1 patients are prone to diabetic ketoacidosis.

1.3.2. Type 2 Diabetes Mellitus

This is the most common form of diabetes, characterized by disorder of insulin action and insulin secretion. These individuals are resistant to insulin action. These form of diabetes often remain undiagnosed for several years because hyperglycemia is not severe enough to manifest in symptoms. However, microvascular and macrovascular changes begin much earlier and initial presentation may be of one of the long term complications.

Majority of these patients are obese with excess trunkal fat deposition.

1.3.3. Other specific types of Diabetes Mellitus

1.3.3.1. Genetic defects in beta cell function

There are several forms of beta cell function defect resulting in diabetes. The common genetic defects are:

- Mutation in chromosome 12 in hepatic nuclear transcription known as HNF-1 alpha
- Mutation at glucokinase gene on chromosome 7p
- Mutation at HNF-4-alpha gene on chromosome 20q
- Mutation in the IPF-1 on chromosome 13 resulting in pancreatic agenesis

1.3.3.2. Genetic defect in insulin action

Genetically determined defects in insulin action are some rare causes of diabetes. Leprechaunism and Rabson-Menderhall syndrome are syndromes seen in children with mutation in insulin receptor gene.

1.3.3.3. Diseases of endocrine pancreas

Extensive injury of the pancreas due to any disease process result in diabetes. Following are some acquired processes:

- Pancreatitis
- Trauma
- Infection
- Adenocarcinoma
- Cystic fibrosis
- Haemochromatosis

It must be noted that even if a small part of pancreas is involved with adenocarcinoma, it result in diabetes.

1.3.3.4 Endocrinopathies

Excess secretion of hormones that antagonize action of insulin like growth hormone, cortisol, glucagon, epinephrine and thyroid hormone result in diabetes. These disease conditions are as follows:

- Cushing's Syndrome
- Acromegaly
- Pheochromocytoma
- Glucagonoma
- Thyrotoxicosis

1.3.3.5 Drugs and Chemicals

Several drugs and chemicals impair insulin secretion. Certain poisons like Vacor (rat poison) and pentamidine destroy beta cells. Many drugs and hormones like nicotinic acid, glucocorticoids impair insulin action.

1.3.3.6 Infections

Certain viruses like Cytomegalovirus, Mump, Rubella, Coxsackie's B are known to be associated with beta cell destruction.

1.3.3.8 Other uncommon form of immune-mediated diabetes

Diabetes may occur due to several other rare immune mediated disorders that result in changes unlike that seen in Type 1 diabetes. Some of the conditions are as follows:

- Stiff Man Syndrome: Stiffness of axial muscles and painful movements with antibodies against insulin
- Anti-insulin receptor antibodies causing diabetes.

1.3.3.7 Other genetic syndromes associated with diabetes

Several genetic syndromes result in diabetes. These are Down's Syndrome, Turner's Syndrome, Klinefelter's Syndrome, and Wolfram's Syndrome etc.

1.3.4. Gestational Diabetes Mellitus

Carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition in pregnancy is known as Gestational Diabetes Mellitus. Pregnant women who have Impaired Glucose Tolerance, Impaired Fasting Glucose and Diabetes Mellitus are classified as Gestational Diabetes Mellitus and they must have one more OGTT at six weeks after delivery.

Blood sugar is normally lower in first trimester of pregnancy. If it is detected to be higher, the pregnant mother possibly was harboring diabetes from pre-pregnancy period.

Women with a history of large for gestational age baby, older women, previous history of glucose intolerance and family history of glucose intolerance are at high risk of developing gestational diabetes.

1.4 Diagnostic criteria for Diabetes Mellitus

Diabetes may present with classical symptoms of severe thirst, polyuria and rapid weight loss. In these patients, blood glucose concentration is grossly elevated in the presence of marked glycosuria. Diagnosis is confirmed by blood glucose estimation. Random whole blood glucose concentrations exceeding 200 mg% or fasting glucose concentration exceeding 126 mg% are considered diagnostic. When such symptoms and signs are absent and blood glucose levels are less markedly elevated, estimations of glucose in fasting or after a carbohydrate load, is necessary to confirm the diagnosis. A diagnosis of diabetes in an asymptomatic subject should never be made on the basis of a single blood glucose value. At least one additional blood glucose test result with a value in the diabetic range is essential.

Criteria for diagnosis of diabetes mellitus:

- Symptoms of diabetes and random plasma glucose concentration >200 mg/dl. Random is defined as any time of day with regard to time of last meal. Classical symptoms are polyuria, polydipsia, polyphagia and unexplained weight loss.
- Fasting blood sugar > 126 mg/dl. Fasting is defined as no calorie intake for atleast 8 hours.
- Two hours post-glucose blood sugar > 200 mg/dl during an OGTT.

Commonly oral anhydrous glucose load of 75g in 250 ml of water is given to adults; fasting and 2 hours post glucose intake blood values of sugar are considered to be a major diagnostic value. In children the glucose load is 1.75g/kg body weight (to a maximum of 75g).

1.5 Impaired glucose tolerance (IGT) and Impaired Fasting Glucose(IFG)

An intermediate group of subjects are recognized whose glucose level do not meet the criteria of diabetes but are too high to be considered normal.

- Normal fasting glucose: FPG <100 mg/dl
- Impaired Fasting Glucose (IFG): FPG > 110 mg/dl but < 126 mg/dl
- Diabetes (provisional): FPG >126 mg/dl

With oral glucose tolerance test, following categories of clinical stages are recognized.

- 2 hour post glucose load < 140 mg /dl : Normal Glucose Tolerance
- 2 hour post glucose load 140- 199 mg/dl: Impaired Glucose Tolerance (IGT)
- 2 hour post glucose load >200 mg/dl : Provisional Diabetes

1.6. Remember the following

Identify high risk group. Greater the number of risk factors present in an individual, greater the chance of that individual developing diabetes. Screen such individual for diabetes.

Following group of individuals are at risk of developing diabetes

- Family history of diabetes
- Obese individuals
- Age >40 years
- Person previously identified IGT
- Individuals using certain drugs like steroid, oral contraceptive, thiazide diuretic
- Individuals having Hypertension
- Individuals having Hyperlipidemia
- Physically inactivate individuals
- Women with a history of GDM or birth weight of over 4 kg.

Chapter 2

Type 1 Diabetes

Type 1 Diabetes

Dr. B.R. Giri MD.

Type 1 Diabetes is a chronic and irreversible disease of any age, characterized by severe deficiency of insulin and dependence on exogenous insulin to sustain life. These individuals cannot survive without insulin replacement. They die due to ketoacidosis.

2.1. Onset

Incidence is approximately 2.5 times higher in the age group of 5-9 years and 3 times higher in the age group of 10-14 years compared with the age group of 0-4 years. Incidence increases from birth to 14 years reaching a peak at the age 11-13 years. Incidence in adult age group is low though it varies from population to population. A large proportion of Type 1 diabetes patients (25-50%) are diagnosed by the age of 15 years whereas only 10-15% manifest with Type 1 diabetes after 40 years of age. Incidence of Type 1 diabetes varies in different countries with 0.1 to 4.6 per 100,000 people in China to 49 in 100,000 in Finland. In most developing countries, Type 1 Diabetes make < 5% of total diabetes population. This holds true for Bhutan.

Diabetes is seen more commonly in men in Europe and USA and in women in Asia and Africa.

2.2. Aetiopathogenesis

There is almost complete lack of insulin secreting beta cells and **absolute insulin lack** is the key defect in type 1 DM. Hyperglycemia *starts abruptly and these individuals invariably present with typical symptoms of diabetes.*

If these individuals do not receive appropriate treatment with insulin, acute complications, primarily ketoacidosis, set in and result in death of the individual over a short period of time. Insulin lack is present from the time of clinical onset of disease and persists throughout the entire clinical course. Some residual beta cell function may be seen (as demonstrated by C-peptide study) and transient periods of remission can occur producing the so-called 'honeymoon' phase of the disease.

The decrease or loss in insulin secretory capacity is due to **actual loss of beta cell mass**. Certain genes present in the short arm chromosome number 6 are found to be associated with Type 1 diabetes. HLA B8, B15, HLA DR3 and DR 4 are described to be associated with Type 1 diabetes.

2.3. Clinical Features

Classical symptoms of Type 1 diabetes are polydipsia, polyuria, polyphagia, overwhelming tiredness and significant weight loss. Other minor symptoms include muscle cramps, various types of bacterial and fungal infection, blurred vision etc. Nausea, vomiting and drowsiness usually indicate impending ketoacidosis and possible coma. Duration of symptoms is short, lasting usually 2-3 weeks or less. Some individuals may present with diabetic ketoacidosis for the first time.

2.3.1. Symptoms linked to osmotic diuresis

Osmotic diuresis result in the following common symptoms

- Polyuria, nocturia
- Increased thirst
- Drowsiness and dehydration

2.3.2. Symptoms and signs linked to lack of insulin

Following are signs and symptoms that are associated with lack of insulin and resultant hyperglycemia.

- Blurred vision
- Hyperglycemia
- Extreme fatigue
- Muscle wasting, weight loss
- Ketoacidosis
- Skin infections, pruritus vulvae

2.3.3. Symptoms linked to calorie depletion

Prolonged hyperglycemia and lack of insulin lead to progressive calorie depletion and features associated to this are:

- Increased appetite
- Weight loss

2.4. Outcome of Type 1 Diabetes

Majority of Type 1 diabetes die early due to infection and acute metabolic complications (DKA). If not treated properly, they do not live long enough to develop life threatening vascular complications. Major causes of death of Type 1 diabetes below the age of 20 is due to acute metabolic complications. After a few years, diabetic nephropathy predominates, contributing to 50% of mortality. Cardiovascular disease accounts for only 10% of death which is 12 times more than in non diabetic for same age. Type 1 patients of early onset are also susceptible to other microvascular complications like retinopathy and neuropathy.

One percent of Type 1 diabetes die in the first year and 33% after 30 years of diagnosis. Risk of death is similar to non diabetics before 20 years of age but it increases by 20 fold after 20 years of age. Good glycaemic control and control of other environmental factors may result in optimal life expectancy.

2.5. Remember the following

- Immunize all children in their first year of life.
- Advise exclusive breast feeding to all children for the first 6 months of life
- In those children diagnosed as having Type 1 diabetes, explain the importance of insulin to the parents and advise against omitting the injection under any circumstance
- Ensure regular follow up
- Psychological support and behavior therapy will help the patient party to adhere to diet and life style modifications
- Withdrawal of a single dose of insulin may result in Diabetic Ketoacidosis

Chapter 3

Type 2 Diabetes

Type 2 Diabetes

Dr. B.R. Giri MD.

Type 2 Diabetes is the commonest form of diabetes, comprising 85 to 95% of diabetes.

3.1 Background

Type 2 Diabetes is a chronic and complex disorder which adversely affect both longevity and quality of life due to multiple, potential serious complications. Type 2 Diabetes is a nonketotic form of diabetes and it usually occurs after the age of 30 years. A strong genetic predisposition is evident. Most individuals are obese and have resistance to insulin action. Endogenous insulin production is usually adequate to avoid ketoacidosis, and it is not required for survival. A vast majority of diabetics are Type 2. It accounts for more than 95% of diabetes in Bhutan. It has a more insidious onset than Type 1 diabetes. It is generally perceived that Type 2 Diabetes is less a serious disease.

However, there is growing evidence that the pathological features of Type 2 Diabetes are of profound importance in the initiation of a cluster of degenerative diseases, including cardiovascular disorders.

Type 2 Diabetes is responsible for 85% of all cases of diabetes in developed countries and in nearly all cases in developing countries. High prevalence is seen in populations who have changed from a traditional life style to a modern one.

Diagnosis of Type 2 Diabetes can be established when classic symptoms accompany, and when diagnostic criteria are met in asymptomatic individuals. Screening is important in patients with a family history of diabetes, significant obesity, recurrent skin, genital or urinary tract infections, physical inactivity or birth weight greater than 4 kg.

Symptomatic patients with polyuria, polydipsia, and weight loss can be diagnosed when random plasma glucose is > 200 mg/dl. When glucose is less than 200 mg/dl, testing as for asymptomatic patients is usually warranted.

In asymptomatic patients, diagnostic testing should be performed when an abnormal screening is obtained or when a strong clinical suspicion of diabetes exist. These tests should be repeated and abnormal results should be demonstrated on more than one occasion for establishment of a diagnosis.

3.2 Type 2 Diabetes: Subgroup

Type 2 diabetes can be classified into obese and non obese subtypes on the basis of their body weight.

3.2.1. Obese Type 2

In developed countries up to 85% of Type 2 diabetes patients are obese. These patients have insensitivity to endogenous insulin that is positively correlated with presence of an abdominal distribution of fat, producing an abnormally high waist-hip ratio. In addition, distended adipocytes and over nourished liver and muscle cells may also resist the deposition of additional glycogen and triglycerides in their storage depots.

Hyperplasia of pancreatic beta cells is present and probably account for normal or exaggerated insulin response to glucose and other stimuli seen in milder forms of disease. In more severe cases, secondary (but potentially reversible) failure of pancreatic cell secretion may result after exposure to persistent hyperglycemia. This phenomenon has been called “desensitization”. It is selective for glucose, and beta-cell recover sensitivity to glucose stimulation once sustained hyperglycemia is corrected by any form of therapy, including diet, suphonylureas, insulin and physical activity.

A major cause of observed resistance to insulin in target tissues of obese patients is believed to be a post receptor defect in insulin action. This is associated with over distended storage deposits and a reduced ability to clear nutrients from the circulation after meals, consequent hyperinsulinism can further enhance insulin resistance by down regulation of insulin receptors.

Furthermore, when hyperglycemia becomes sustained, a specific glucose transported protein in insulin target tissue also becomes down regulated after continuous activation. This contributes to further defects in post receptor insulin action, thereby aggravating the hyperglycemia.

When over feeding is corrected, the storage depots become less saturated and the cycle is interrupted. Insulin sensitivity improves and is further normalized by a reduction both of the hyperinsulinism and hyperglycemia.

3.2.2 Non-Obese Type 2 Diabetes

Upto 15% Type 2 Diabetics are non-obese. In most of these patients, impaired insulin action at the post receptor level and an absent or delayed early phase of insulin release in response to glucose is demonstrated.

Hyperglycemia in patients with non-obese Type 2 Diabetics often respond to dietary therapy or to oral hypoglycemic agents. Occasionally insulin therapy is required to achieve satisfactory glycemic control even though it is not needed to prevent ketoacidosis.

3.3 Clinical Features of Type 2 Diabetes

Type 2 Diabetes may present with characteristic signs and symptoms. The presence of obesity or a strong positive family history of mild diabetes also suggests a high risk for development of Type 2 Diabetes.

3.3.1 Symptoms

Classic symptoms of polyuria, thirst, blurred vision, paresthesia and fatigue are manifestations of hyperglycemia and osmotic diuresis. However, many patients with Type 2 diabetes have an insidious onset of hyperglycemia and may be relatively asymptomatic initially. This is particularly true in obese patients, whose diabetes may be detected on routine laboratory tests. Chronic skin infections are common. Generalized pruritus and symptoms of vaginitis are frequently the initial complaints in women.

Diabetes should be suspected in women with chronic candidial vulvo-vaginitis as well as in those who have delivered large infants (birth weight > 4kg) or have polyhydramnios, pre-eclampsia or unexplained fetal losses. Occasionally patients with previously undiagnosed diabetes may present with impotence.

3.3.2 Signs

Non-obese patients with mild form of diabetes often have no characteristic physical findings at the time of diagnosis. Obese diabetics have any variety of fat distribution. However, diabetes is more often associated in both men and women with localization of fat deposits on the upper part of the body (particularly in the abdomen, chest, neck and face) with relatively less fat on the appendices, which may be quite muscular. This centripetal fat distribution (android) result in high waist to hip ratio.

Mild hypertension may be present in obese diabetics, particularly when android form of obesity is predominant. In women, vulval candidiasis with reddened, inflamed vulvae may be the initial presentation of Type 2 Diabetes.

3.4. Type 2 diabetes in Children

Most Type 2 Diabetes present after 40 years of age with peak age of onset being 60 to 70 years of age. However, it has been increasingly observed that Type 2

Diabetes is seen in children and adolescents as well.

Like in the adults, sedentary life-style and obesity are the main contributing factors of the disease. These children have a strong family history of diabetes and the disease presents at around 15 to 16 years of age. There is a strong association with insulin resistance.

3.5. Remember the following

- Type 2 Diabetes usually occurs above 30 years of age.
- It has an insidious onset
- Most Type 2 Diabetics are silent, detected on routine examinations or present with complications
- Insulin secretion and action defects present in varying degree

Chapter 4

Principles of Management of Diabetes Mellitus

Principles of Management of Diabetes Mellitus

Dr. B.R. Giri MD.

4.1. Aims

The aims of optimal management of diabetes are as follows

- Correct and normalize metabolic derangement
- Maintain standard body weight
- Prevent, **revert, delay or minimize complications**
- **Maintain a healthy & productive life.**

4.2. Management of Diabetes entails the following

Diabetes is life long metabolic disorder. It does not get cured hence diabetics must follow the following to have an optimal control of the disease and prevent or delay its complications from occurring.

- Diet regulation
- Regular scheduled exercise
- Use of antidiabetic agents
- Disciplined life style.

4.3. Diet in Diabetes

Diet modification and its regulation is one of the most important aspects in diabetes management.

- a) To normalize and maintain normal blood sugar level to prevent or delay complication
- b) To meet nutritional needs
- c) Maintain ideal body weight
- d) To maintain normal growth rate
- e) To achieve optimum nutrition in pregnancy and lactation.

Refined carbohydrates like glucose, sugar, sweets should be avoided. Fat and proteins can be consumed as usual unless restricted. A sedentary person needs 30kcal/kg body weight whereas a hard worker requires 35kcal/kg of calories a day. Underweight diabetes will require higher calories and obese require lesser (800-1200kcal/day). Sufficient vegetables and fibers in diet are recommended. Suggested calorie distribution is 12-20% from protein, 50-60% from carbohydrate and 20-30% from fat (<10% from saturated fat). Diabetics should know the importance of diet. Diet should be reviewed if blood sugar remain uncontrolled, weight loss or gain occur.

4.4. Physical Activity

Physical activity controls hyperglycemia, hyperlipidaemia, sensitizes insulin receptors, improves circulation, prevents atherosclerosis, reduces blood pressure, increases work capacity and the person feels a sense of well being and has improved quality of life. Physical activity reduces need of antidiabetic agents. Good glycemic control can be achieved by a delicate balance of diet management, physical activity, relaxation and hypoglycemic agents. Once blood sugar control is achieved, a balance of these activities should be maintained to achieve continued glycemic control unless other emergent situations arise like acute infections.

4.5. Use of antidiabetic medications

All Type 1 Diabetics need daily insulin supplementation. Diabetics must learn to use insulin by themselves. Most Type 2 Diabetics require taking oral blood sugar lowering agents, the dosage of which is adjusted according to blood sugar control. Use of these agents can result in serious complications like hypoglycemia, the features of which patients and immediate relatives must know.

4.6. Disciplined life style

Diabetes is life long metabolic disorder. Control of blood sugar will cease to occur if one of the three aspects of its management viz. dietary control, physical activity or use of medication is discontinued. Hence diabetics themselves and their family members must understand the situation and work towards continuing diabetes control measures for life time.

Chapter 5

Diet in Diabetes

Diet in Diabetes

Dr. B.R. Giri MD.

Food is an important part in the management of diabetes. This has been realized for a long time as the cornerstone of diabetes management. Diabetes is a life long disease and hence, diet modification must be carried on for lifetime. The nutritional needs of a diabetic remain the same as when he/she has been in non-diabetic state. A nutritionally balanced diet is required in a diabetic as in a non-diabetic. A non-diabetic can take any type of food at any time of the day in any amount and it will not cause abrupt rise in blood sugar whereas a diabetic must be careful about his/her diet as this can result in high post-food rise in blood sugar.

5.1. Modern eating

One notices changing eating habits with improvement in socio-economic conditions and urbanization. This plays a major role in causation of diabetes in an individual who has other risk factors for diabetes.

5.1.1. Factors responsible in changed eating habit and life-style

- Shift in (urban) eating preferences
 - Increased income has a direct bearing on family's expenditure on food.
 - Desire for quality family time culminating in less home cooking and eating outside
 - Availability of processed food
 - Mass media campaigns
- Increase in sedentary life-style

5.1.2. What is wrong with modern diet?

There is a direct mismatch between calorie need and calorie intake in modern diet and hence extra calories get deposited as fat in the body.

Modern living with limited physical activity does not need the amount of food one eats nor food which is:

1. Refined – high simple sugar
2. Rich in Calorie
3. Rich in fat

This is the type of food that is eaten normally and it has direct health bearing.

5.1.3. Social influences in eating habits

Society greatly influences eating habit. Food is served in almost all social occasion. It is customary to serve food in excess.

- Food serves as a source of pleasure in life
Family get-together and celebrations like birthdays, anniversaries, festivals, or success are celebrated with rich food.
- Being overweight or well fed is recognised as a sign of prosperity in many societies.
- Hospitality result in over feeding.
- Calorie dense foods like oily, fatty and sweet food are perceived as the best food
- Concomitant alcohol use result in over eating
- Modern life requires eating out
 - Work, parties
 - Too tired to cook, so “take home” meal is ordered

5.1.4. Unhealthy food habits

Increased fat and carbohydrate intake result in excessive weight gain in an individual. Certain food item that have large amount of fat and carbohydrate that have to be avoided are as follows.

- Curries cooked in excess of oil
- Deep fried foods
- Fast foods
- Too sweet beverages
- Sweets, biscuits, cake, chocolate, sweet meat
- Excess of refined food e.g. sugar based
- Excess of fizzy drinks
- Increased intake of processed foods
- Excess consumption of polished rice
- Increased intake of biscuits, bread, mixtures, soft drinks
- Less intake of vegetables and fruits
- Excess of salt (in processed food)
- Increasing alcohol consumption

If unhealthy eating and life style is causing this massive epidemic of diabetes and obesity then it should be possible to prevent it by a healthy life-style.

5.2. Importance of Nutrition management

Diabetes is a metabolic disorder affecting food (carbohydrate, fat and protein) metabolism. Nutrition therapy should be an integral part of its management. Diet management is the corner stone in diabetes management. It is an effective tool in combination with physical exercise and is preferable to pharmacological therapy to begin with, for patients with IGT, those at risk of, or are in early

stages of Type 2 diabetes.

Inappropriate nutrition can make best planned pharmacological intervention ineffective.

5.3. Principles of Nutrition management

Following are some important principles of nutrition management.

- Provide appropriate energy and nutrients for health, growth and activity
- Preserve social and psychological well-being
- Reduce symptoms of diabetes
 - Attain and maintain euglycemia
 - Prevent hypoglycemia and hyperglycaemia
- Achieve and maintain acceptable body weight
- Attain and maintain normal lipid levels
- Attain and maintain acceptable blood pressure levels
- Prevent, delay or treat micro and macrovascular complications of diabetes
- Complement drug and insulin therapy
 - Nutrition advice cannot be independent of drug/insulin regimen

5.3.1 How can these be achieved

Nutrition management can be achieved by involving the patient as well as the family members. It is crucial to involve the family members as without their support, patient alone can not sustain life style changes required of him/her. All nutritional advice should be patient centered.

- Individualized assessment
- Appropriate for age, sex, weight, life-style, personal, economic, social and cultural circumstances
- Takes into account readiness to change

5.3.2. Diet recommendations in diabetes

Food contains calories through carbohydrate, fats and protein. Salt and important vitamins and minerals are also supplied through food. Diabetics require the same food as when diabetes was not contracted. However, proportion of different food must be readjusted. Following are recommended food allowance for people with diabetes. However, food must be individualized.

- Carbohydrates: 50-65% (mostly starchy) of daily calorie requirement
- Fats: 20-35% of daily calorie requirement
 - saturated fat <10%
 - polyunsaturated fat <10%
 - monounsaturated fat >10%
 - cholesterol < 300 mg/day

- Protein: 10-20% of daily calorie requirement (0.8 g/kg/day)
- Sodium: < 3000 mg /day
- Vitamins & Minerals: with balanced diet, supplementation not needed
- Dietary fibers: minimum 20g /1000 kcal

5.4 Carbohydrate recommendations in diabetes

Carbohydrate is the primary source of calories in diet.

- 50-65% of energy must be derived from carbohydrate
- The amount and source of carbohydrate should be considered when planning meal
- Carbohydrates should come mainly from
 - whole grains (wheat, rice, corn, millet, maize, buckwheat)
 - legumes, pulses
 - fruits and vegetables

5.4.1. Sucrose (Sugar)

White or table sugar is constituted of sucrose. This has either to be avoided or used in moderation.

- Sucrose intake is allowed up to 10% of total daily energy
- Evidence suggests that dietary sucrose does not increase glycemia more than isocaloric amounts of starch.
- Excess sucrose must be substituted for other carbohydrate sources in food/meal plan or, it must be adequately covered with insulin or other glucose lowering medication.
- Advice against sugar in drinks as this result in rapid increase in blood sugars.
- Encourage use of low or reduced or no added sugar products

5.4.2. Foods rich in Carbohydrate

Following food items contain ample amount of carbohydrate. These have to be used in moderation.

- Rice, puffed rice, rice flakes (*ship*) and potatoes, *zaw*
- Wheat flour, maize flour, millets, buckwheat flour
- Fruits, fruit juice and vegetables
- Potatoes, tapioca, sweet potatoes
- Bread, cake, biscuits
- Pulses -whole and split
- Lentils,
- Soft drink, fizzy drink

5.4.3. Food rich in simple sugars

These following food contain simple sugar. Simple sugars are readily absorbed from gut and result in post food hyperglycemia.

- Sugar, sugar cane juice
- Sweets and sweet meat
- Biscuit
- Sugar in tea and coffee
- Milk dessert
- Soft drink

5.5. Protein recommendation in diabetes

Protein is normally required for growth and maintenance of wear and tear besides other vital functions of body.

- High intake of animal protein is not encouraged because these foods are also high in fat
- Protein must constitute 10 - 20% of total calories per day similar to normal population
- Recent recommendation of protein in diabetic is 0.8 grams /kilogram body weight/day

Protein requirement is increased in children, pregnant and lactating mother and in certain medical conditions.

5.6. Fat recommendation in diabetes

High fat diet is related to hyperlipidemia and other related diseases. Fat intake need to be individualized. Fat is generally saturated and unsaturated. Animal fat is mostly saturated. Palm and coconut oil are saturated too. Olive and peanut oil are monounsaturated and have least effect on blood lipid. Polyunsaturated fat in vegetable oils such as corn, sunflower, and these probably lowers plasma cholesterol level.

- Diet should be low in fat with particular emphasis on the type of fatty acid
- Fat must constitute 20-35% of total calories
 - o Low Saturated < 10%
 - o Low Polyunsaturated (PUFA n - 6) up to 10 %
 - o High Monounsaturated (MUFA) > 10%
 - o Low Trans fatty acid intake
 - o Low cholesterol < 200 mg/day (less animal products, cheese, egg yolk, butter)

5.6.1. Types of fat

Food may contain visible fat that is fat added during cooking and invisible fat that is naturally present in food.

Different types of fat and food that contain these fat are as follows:

- Saturated fat : red meat, butter, cheese, margarine, hydrogenated fat, ghee (clarified butter), whole milk, cream, lard
- Polyunsaturated : Safflower oil, sunflower oil, corn oil
- Monounsaturated : Olive oil, canola oil, rape seed oil, groundnut oil, mustard oil, sesame oil
- Cholesterol : Red meat, egg yolk, cheese, butter, cream, organ meat, ghee (clarified butter)
- Trans-fatty acids : Biscuit/cookie, cake, sweet meat, ready to eat snacks

Trans fatty acid is formed when liquid fat, such as oil, is chemically hydrogenated. Trans fat raise LDL cholesterol and lowers HDL cholesterol. Hydrogenated fat like dalda is the main source of trans-fat consumed. Smaller amount of naturally occurring trans-fat is in meat and milk.

Table 5.1 : Fat and oil

Fat Distribution in commonly used oil. Fatty-acid (grams/100grams)				
	Saturated Fatty Acid	MUFA	PUFA (_-6)	PUFA (_-3)
Olive oil	13	76	10	1
Peanut oil	18	48	34	<0.5
Canola oil	6	58	26	10
Rapeseed oil	8	70	12	10
Sesame oil	15	42	42	1
Corn oil	12	32	55	1
Cottonseed oil	22	25	52	1
Soyabean oil	15	27	53	5
Sunflower oil	13	27	60	<0.5
Safflower oil	13	17	70	<0.5
Coconut	90	7	2	<0.5
Vanaspati	24	19	3	<0.5
Ghee	65	32	2	<1.0

5.7. Fibre

Dietary fibre is a portion of plant food and it is not digested in human intestine. It has various important properties like viscosity, water holding capacity, bile acid binding capacity. Degradation of the fibre by microbes in colon forms gel in gastrointestinal tract that slows absorption of glucose and lipid, slower stomach emptying, delay intestinal transit. Fibre rich diet improve glucose tolerance, lower total cholesterol, LDL cholesterol and triglyceride.

A high fibre diet is recommended in all diabetics.

- Fibre is recommended similar to normal individuals
Total of 20-35 grams per day
10 - 25 grams of soluble fibre daily
- Insoluble fiber sources:
wheat bran, whole grain, seed, fruit & vegetable
- Soluble fibre sources:
Legume (bean), oat bran, barley, apple, citrus fruit, potato

5.8. Minerals and vitamins in diabetes

Minerals and vitamins are contained in food that one eats every day. However, supplementation is necessary under certain circumstances

- Multivitamin supplementation is needed for
Pregnant woman
Lactating woman
Elderly
People on strict energy restriction
Critically ill
Renal disease
Poor metabolic control
Nutritional deficiency

5.9. Trace elements

A balanced diet is required to supply all minerals and trace elements for health.

- They are inorganic substances that regulate many vital processes within the body
- They are found in blood, enzymes, hormones, bones, skeleton, teeth and tissue fluid
- Calcium supplementation is required for elderly. A daily intake of 1,000–1,500 mg is required.

5.10. Alcohol

Alcohol must not be consumed more than recommended for a healthy individual. Chronic ingestion of alcohol can result in chronic pancreatitis and diabetes.

- Alcohol intake must be same as for general population
 - one drink per day for women
 - two drinks per day for men
- Alcohol should be consumed with meal to prevent hypoglycemia
- Alcohol must be avoided in pregnancy, pancreatitis, severe dyslipidemia, neuropathy and alcohol abuse

5.11. Planning meal

Every diabetic must have his/her meal planned. The meal must not be exotic but should take into consideration the patient's habits, likes and dislikes and cultural and individual acceptability.

- Determine patient's food habit by 24 hour recall of food frequency and ascertain different food the patient was generally taking.
- Estimate calorie requirement of the patient by BMI, physical activity level and any special conditions like illness, pregnancy, lactation.
- Diabetics must know the importance of diet from the time of detection of disease.
- "Once a diabetic, one is always a diabetic for life". So proper education is most essential part of management of diabetes
- If a diabetic is unable to take food, liquid food like milk, barley, soup, 'thuep' must be given at hourly interval.

Table 5.2 Calorie requirement for adults

Persons with Diabetes	Daily Calorie/Kg body weight
Sedentary with normal body weight (BMI 18.5 to 25)	30
Moderate To strenuous physical activity with normal BMI	35 to 50
Pregnancy First trimester	28 to 32
Pregnancy Second trimester	36 to 38
Pregnancy Third trimester	36 to 38
Lactating	36 to 38
Obese, Sedentary women BMI >25	20

Underweight: BMI less than 18.5

Add 300 to 500 calorie / day to basal requirement.

Juvenile:

Child one year age: 1000 to 1100 calorie/day

Child more than one year: Add 100 calories for each year

Add or subtract 25% of total calculated calories for activity or inactivity respectively. Add 25% of calorie requirement for age for adolescence.

Gestational Diabetes Mellitus

Add 300 calories/day over basal allowance from second trimester. If obese, do not add calories from the requirement. If underweight, add calories and at least 20 gms. proteins

Determine the amount, type and distribution of fat, carbohydrate and protein.

Desirable body weight in adult

BMI

20 to 23	Ideal
< 16	Underweight
16 to 18.5	Probably underweight
18.5 to 25	Probably well nourished
25 to 30	Possibly obese
>30	Obese

5.12. Dietary strategy

5.12.1. Type 2 Diabetes/Impaired Glucose Tolerance

5.12.1.1. Obese/ Overweight (BMI>25)

- Hypocalorie diet with high fibre.
- Same distribution of carbohydrate, protein and fat in diet as for others.

5.12.1.2. Normal weight (BMI 18.5 to 25)

- Adequate calories and adequate spacing between meals.

5.12.1.3. Underweight (BMI< 18.5)

- Extra calorie
- Small frequent feeding

5.12.2. Type 1 Diabetes

5.12.2.1. Juvenile

- High calories and protein
- If obese, less calorie from usual requirement
- Increased frequency of feeding
- Adjustment of calories each year

5.12.2.2. Adult

- Adequate calories
- Low calories for obese
- Adequate spacing between meals
- Even distribution of calories in meals
- Almost same amount of food every day
- Keep timing of meals constant everyday

Chapter 6

Oral Hypoglycemic Agents (OHA)

Oral Hypoglycemic Agents (OHA)

Dr. B.R. Giri MD.

6.1 Introduction

Near total insulin deficiency occurs in Type 1 Diabetes and hence, this condition requires replacement of insulin. In Type 2 Diabetes, relative insulin deficiency occurs. There is significant insulin resistance as well. Insulin resistance and deficiency in different degrees in combination are the major components in pathogenesis of Type 2 Diabetes.

There is gradual but progressive loss of beta cell function in the course of natural history of Type 2 Diabetes that dictates the physician to change treatment from time to time.

Table 6.1. Target of control in diabetes

Self monitored blood glucose	>50% of self monitored blood glucose values within target range
Blood glucose	Pre-meal : 80 to 126 mg/dl Post-meal: (2 hrs. after meal): <160 mg/dl Bed time: 100 to 160 mg/dl
Glycosylated Haemoglobin (HbA1c)	Normal 6%, Target : <7% Frequency every 3 months
Blood Pressure	<130/80 mm Hg.
Lipid	LDL <100 mg/dl, HDL > 40 mg/dl, Triglyceride <150 mg/dl

6.2. Goals of Management

Oral hypoglycemic agents are those drugs which when given orally in patients with Diabetes Mellitus can effectively correct the derangement of carbohydrate, protein and fat metabolism developed during disease process.

The goals of management of diabetes are

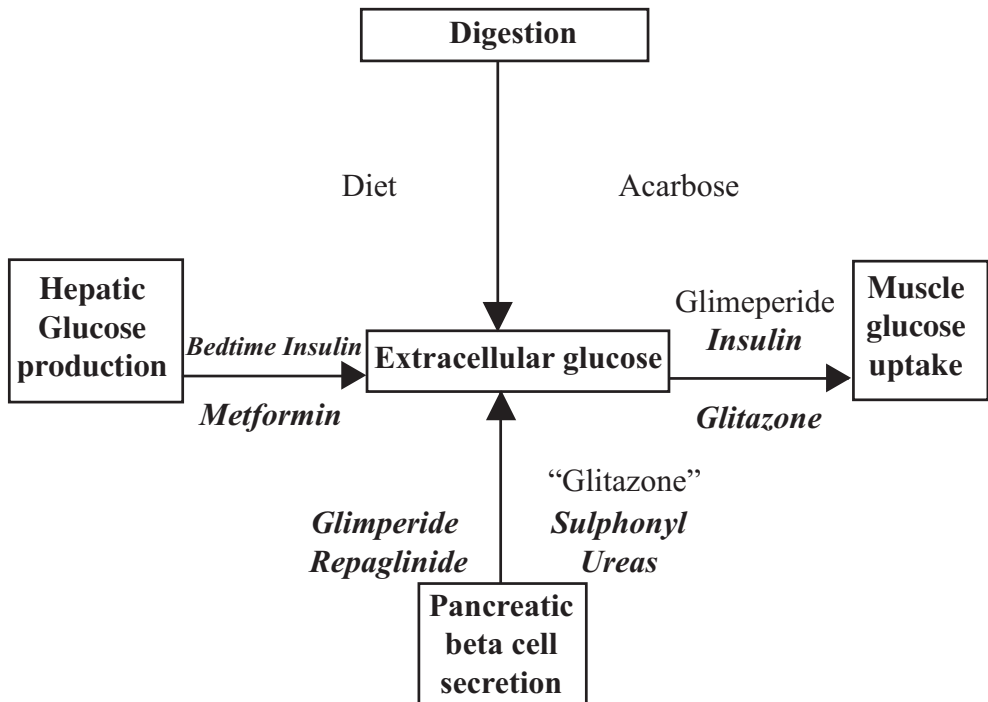
- Relief of symptoms
- Correction of blood chemistry value
- Slowing and /or prevent macro and micro vascular complications
- Restoration of sense of well being
- Maintenance of ideal body weight
- Good pregnancy outcome

6.3. Classification of oral hypoglycemic agents

There are three categories of oral hypoglycaemic agents available.

- **Insulin secretagogue:** Improves insulin availability in the body.
 - ♦ Sulphonyluria
 - ♦ Non-sulphonyluria
 - Repaglinide
 - Nateglinide
- **Insulin sensitizer:** Improve insulin action or reduce insulin resistance
 - ♦ Metformin
 - ♦ Thiazolidinedione
- **Alpha glucosidase inhibitor:** Reduce glucose absorption from the gastrointestinal tract.

6.4. Site of action of Oral Hypoglycaemic Agents



No drug is available which can act at all points spontaneously

6.5. Insulin secretagogues

6.5.1. Sulfonyluria

6.5.1.1. Absorption

Sulfonylurias are completely absorbed from gastrointestinal tract into blood. Like other drugs, absorption process may be delayed by fiber-rich diet. In blood up to 75-95% of drug is bound to protein. So bio-availability may be influenced by protein deficiency and by drugs competing for the same albumin.

Sulfonyluria metabolites are excreted primarily by kidney. In liver and kidney diseases the drug or its metabolites may accumulate in blood and thus increase risk of prolonged hypoglycemia.

Table 6.2 Pharmacokinetics of current Sulfonyluria

Drug	Peak level in plasma(hrs)	Duration of action(hrs)
Chlorpropamide	2.4	60
Glipizide	1.3	Up to 24
Glybenclamide	4	Up to 24
Gliburide	4	24
Gliclazide	2-3	Around 20
Glimeperide	2-3	Around 20

Table 6.3 Pharmacokinetics of current Sulfonyluria

Drugs	Metabolites	Dose/day	Excretion
Chlorpropamide	Active	1	Kidney 100%
Glipizide	Inactive	1-2	Kidney 80%, bile 20%
Glybenclamide	Weakly active	1	Kidney 50%, bile 50%
Gliburide	Weakly active	1	Kidney 50%, bile 50%
Gliclazide	Inactive	1-2	Kidney 60-70%
Glimperide	Weakly active	1	Kidney 60%, bile 40%

6.5.1.2. Mechanism of action of Sulfonyluria (Glibenclamide)

Sulfonylurias stimulate beta cells to secrete insulin. It increases beta cell sensitivity to glucose. It does not increase synthesis of insulin but it helps release of stored insulin. Sulfonylurias inhibit secretion of glucagon from pancreas. It helps in decreasing insulin resistance. It increases tissue sensitivity to insulin. It also increases hepatic and muscle sensitivity to insulin.

6.5.1.3. Dose schedule

Most Sulphonyluria have long duration of action. Hence, single dose schedule is adequate. However, when morning dose exceed 2 tablets, a small dose in the evening must be added.

6.5.1.4. Side Effects

Most important side effect of sulphonyluria is hypoglycemia. In situations of renal failure, hypoglycemia is a troubling side effect.

6.5.1.5. Contraindication

Long acting sulphonyluria can not be used even in mild renal failure (S. creatinine > 2.0 mg/dl)

6.5.2. Non-Sulphonyluria secretagogue

These drugs are secretagogue without sulphonyl moiety and are termed non sulphonyluria.

The secretagogues that are in use are

- Repaglinide
- Nateglinide

Mechanism of Action:

6.5.2.1. Absorption

- These drugs are rapidly absorbed and appears in blood in 5 to 10 minutes following ingestion

6.5.2.2. Metabolism

- Non-secretagogues are metabolized in liver by cytochrome P450 system and 60% excreted in bile
- Elimination occur through faeces in over 90%, Urine 8%, Unchanged in faeces 2% . It is independent of renal excretion. Elimination half life is 0.5 to 1.4 hours.

6.5.2.3. Onset of action

Action begins within 30 minutes of ingestion. The duration of action lasts for 2 to 3 hours.

6.5.2.4. Dose

- Ripaglinide: 0.5 to 4 mg per dose, total 12 mg per day, thrice a day before major meals. Should not receive medicine if meal is skipped.
- Nateglinide: 120 mg before each major meal, three times a day

Advantages

- Correction of post prandial hyperglycemia is better
- Hypoglycemia is averted
- Can be given in mild to moderate renal failure

6.6. Biguanide

6.6.1. Metformin

Actions of biguanides are not well understood but possible mechanisms are as follows. Biguanides reduces gastrointestinal absorption of glucose and enhances uptake of glucose by peripheral tissues in presence of available insulin. It also reduces gluconeogenesis and therefore lower hepatic glucose output. Biguanides stimulate anaerobic glycolysis and increases insulin receptor binding. Metformin reduces raised glucose levels but does not normally cause hypoglycemia

6.6.1. 1. Absorption

- Most absorption occurs through gastrointestinal tract.
- 20 to 30% excreted in stool
- Absorption occur in 1 to 2.6 hour

6.6.1. 1. Metabolism

- Metformin is not metabolized in body

6.6.1. 1. Side effects

- Transient gastrointestinal upset, metallic taste, nausea, anorexia
- Abdominal discomfort, cramp, vomiting, flatulence, diarrhoea
- Lactic acidosis predisposed by renal failure, hepatic failure, alcohol abuse

6.6.1. 1. Contraindication

- Renal impairment with serum creatinine >1.4 mg/dl
- Hepatic dysfunction with ALT > 2 times of normal
- History of acidosis

6.6.1. 1. Dosage

- 250 mg to 3 grams in 3 divided doses half an hour before meals
Advantage
- No hypoglycemia

6.6.2. Thiazolidinediones

Following are some thiazolidinediones that are used in clinical practice.

- Rosiglitazone
- Pioglitazone
- Troglitazone

Anti hyperglycemic effect of these drugs are:

- Dose dependent
- Glucose lowering effect is dependent on availability of insulin
- No effect on insulin secretion
- Improves insulin sensitivity
 - Increase peripheral level glucose disposal by adipose tissue and muscles
 - Decreased hepatic glucose output at the level of liver

6.6.2.1. Absorption

- Peak levels are observed within 2 hours in fasting state and 3 to 4 hours after food.

Mechanism of Action:

6.6.2.2. Metabolism

It is extensively metabolized in liver.

6.6.2.3. Excretion

- Most excretion, 70 to 85% occur through bile
- Renal excretion 15 to 30%
- Serum half life 3- 7 hours
- Duration of action is upto 24 hours

6.6.2.4. Contraindications

Thiazolidinediones must not be used under following circumstances.

- Liver disease
- Pregnancy
- Lactation

6.6.2.5. Dosage

- Single dose 15 to 45 mg half an hour before meal

6.6.2.6. Side effect

- Headache, myalgia, anemia, weight gain, edema

6.7. Alpha-Glucosidase inhibitor

Following are some of the commonly used alpha-Glucosidase inhibitors.

- Acarbose
- Voglibose
- Miglitol

6.7.1 Mechanism of action

- Inhibit carbohydrate absorption by selectively inhibiting disaccharidases in intestinal brush borders.
- Oligosaccharides can not be digested and absorbed hence post-prandial blood sugars not raised

6.7.2. Absorption

- Binds reversibly in the intestinal epithelial wall
- Almost no systemic absorption

6.7.3. Side effects

- Abdominal bloating
- Diarrhoea
- Mal-absorption

6.7.4. Contraindications

- Hepatic dysfunction
- Renal impairment

6.7.5. Dosage

- 25 to 100 mg per dose three times daily

6.8. Remember the following

Ascertain type of diabetes mellitus and reserve function of beta cells of pancreas. Evaluate indications and contraindications of oral hypoglycemic agents for the particular patient. Ensure dietary compliance and physical activities. Start with low dose of sulphonylurea in the morning. Try to control glycemic status slowly. Increase the dose with small increment at 7 days interval or more to a maximum morning dose. When morning fasting glucose is not under acceptable level, add small dose at night.

Chapter 7

Insulin and its Complications

Insulin and its Complications

Dr. B.R. Giri MD.

7.1. Insulin

Insulin is a protein consisting of 51 amino acids with 2 peptide chains, A-chain with 21 amino acids and B chain with 30 amino acids. The two chains are connected together by 2 disulfide bridges.

7.2. Sources of Insulin

- Pancreas derived bovine and porcine insulin
- Human Insulin.
 - a) Derived from human cadaveric pancreas
 - b) End of end synthesis from amino acid. About 200 steps are there in its formation, so supply is inadequate and cost is more.
 - c) Enzymatic semisynthetic process by which porcine insulin is converted to human type
 - d) Bio-synthesis from E.coli, S.C. yeast by employing recombinant DNA technology.

Portion of human insulin gene are introduced to plasmids of E.coli. A & B chains are produced separately and are subsequently linked by disulfide bonds.

7.3. Preparations and Types of Insulin

Table 7.1: Types of Insulin

Type preparation	Action onset (hr)	Peak Profile in hr.	Maximum duration of action
Regular (plain)	$\frac{1}{2}$ -1	2-4	6-8
Lente	2-5	6-14	18-24
Semi Lente	1-3	6-12	12-18
Ultra Lente	4-6	18-24	36-40
Mixtard	$\frac{1}{2}$ -1	6-12	18-24

7.3.1 Short acting (Soluble, Regular, Plain)

Regular insulin has most rapid and shortest duration of action. For optimal effect, it is best taken before meal. It is the only insulin that can be used intravenously. Therefore it is the insulin used in treatment of DKA, surgery and shock. It can be given subcutaneously in combination with an intermediate or long acting preparation. When given S/C, action starts within 30-45 min; peaks at 2-4 hrs and duration of action lasts for about 6 hrs.

7.3.2. Lente Insulin

Lente insulin is intermediate acting insulin. Lente insulin has onset of action of about 2.5 hrs, peak between 6-14 hrs. or longer. Intermediate insulin is given either once or twice a day.

7.3.3. Mixed Insulin

Premixed insulin 30 : 70 (short acting : long acting) are available for Bhutanese patients routinely. However it is also available as 50 : 50(short acting : long acting)

7.3.4. Insulin Concentrations

- Most widely available and used is 100 IU/ml
- Uncommonly used are 40 IU/ml

Insulin must be administered by insulin syringes calibrated to the concentration of insulin being used.

7.4. Storage of Insulin

Insulin can be kept at 2-8°C without loss of its efficacy as long as 3 months. Freezing is avoided. It should be kept away from light. It may be kept at 25°C for one month without loss of potency.

- Never freeze insulin
- Avoid direct sunlight or warming in hot climate
- Store unused insulin in fridge at 2 to 8°C
- After opening an insulin vial, it should be discarded after 3 months if kept at 2 to 8° C or after a month if kept at room temperature
- In hot climate, transport and store it in cooling jar, thermos flask with cold water or wet cloth wrapped around

7.5. Route of Administration

1. Sub-cutaneous route - usually all routine patient taking insulin.
2. Intravenous route - during Diabetic Ketoacidosis.
 - Front or lateral aspect of thigh are preferred site for ease of administration and slower absorption of longer acting insulin
 - Lower abdomen below the umbilicus is the usual preferred site of injection when faster absorptions is required. It is least affected by physical activity
 - Buttocks, upper outer quadrant may be useful in small children
 - Lateral aspect of arm is another preferred site of administrationIt must be remembered that insulin is injected at different sites on different occasions, rotating around different site and returning to the original site only after a month.

7.5.1. Problems with insulin injections

Insulin administration is fraught with certain problems. These have to be looked for at periodic intervals and remedial measures taken.

- **Hypersensitivity:** Hypersensitivity to insulin injections is uncommon. However, when it occurs, it can either be local or systemic. With the newer human insulin it is extremely rare.
- **Lipohypertrophy:** There will be accumulation of fat and fibrous tissues at the site of injection. Avoid injecting repeatedly at the same site.
- **Lipoatrophy:** Atrophy of fat at injection site can occur. However, this is extremely uncommon
- **Painful injections:** If injection is deep to infiltrate muscle, it can be painful. Please check that the patient receives subcutaneous injection.
- **Insulin leakage** is difficult to avoid. Withdraw needle slowly and apply gentle pressure over the injection site.
- **Bruising and bleeding** are commoner with intramuscular injections
- **Bubbles in insulin** must be removed

7.6. Indications for Insulin

- All patients of Type 1 Diabetes
- Patients of any age, acutely decompensated state, DKA, lactic acidosis, or any emergencies like acute MI, surgery, infection etc.
- Pregnancy and diabetes
- Type 2 Diabetes Mellitus
 - Drug failure when, OHAs, diet control and physical activity do not keep sugar levels under control.
 - Emergency situation like surgery, trauma, infections like tuberculosis, boil, carbuncle, hepatitis.
 - Patients with complications like retinopathy, nephropathy.
 - Patients with very high blood glucose at presentation

7.7. Goal of Insulin Therapy

- To preserve life of diabetic patient and to relieve patients from symptoms.
- To enable patient to have as normal and productive life as possible.
- To establish and maintain good metabolic control
- To prevent or at least delay long term complications of Diabetes.

7.8. Target of Control

Fasting blood glucose value should be kept between 90-110 mg/dl and post prandial blood glucose value of below 140 mg/dl and HbA1 C < 6%.

7.9. Daily Requirements.

Daily insulin production in normal person ranges between 24-30 units. Type 1 diabetes patients require generally between 0.5-1.0 insulin units/kg/day.

7.10. Principles of insulin therapy

- To provide sufficient insulin throughout 24 hours to cover basal requirement
- To deliver higher bolus of insulin in an attempt to match the glycaemic effect of meals

7.11. Frequently used schedule for Insulin Administration

- **Two injections** daily of a mixture of short and intermediate acting insulin (Mixtard) before breakfast and main evening meal
Combines insulin: Lente and Regular.
AM dose : Lente + Regular (2/3rd of total daily dose)
PM dose : Lente + Regular (1/3rd of total daily dose)
For both AM and PM doses, 2/3rd of total dose as lente and 1/3rd as plain.
- **Three injections** daily, using a mixture of short and intermediate acting insulin before breakfast, short acting insulin alone before afternoon meal and a long acting insulin at bedtime
- **Basal bolus regimen**, of short acting insulin 20 to 30 minutes before main meals (breakfast, lunch and main evening meal), intermediate or long acting insulin at bed time.
- **Insulin pump** dosages with fixed or variable basal dose and bolus doses with meals

7.12. Guidelines on dosage

- During partial remission phase, daily insulin requirement is < 0.5 IU/kg/day
- Pre-pubertal children usually require 0.7 to 1.0 IU/kg of insulin per day
- During puberty, insulin requirements may rise above 1 IU/kg/day
- Adults require 0.2 to 0.5 IU/kg insulin per day
- Insulin adjustment must be made until target blood glucose is achieved

7.13. Remember the following in using Insulin

- In case of elevated fasting blood sugar, increase pre-dinner or pre-bed time intermediate insulin.

- For rise in post breakfast blood sugar, increase pre-breakfast short acting insulin.
- For elevated blood glucose before evening meal, increase pre breakfast intermediate acting insulin or increase dose of pre-lunch short or rapid acting insulin if on basal bolus regimen
- If a rise in blood sugar after evening meal is noticed, increase pre-evening meal short or rapid-acting insulin

Furthermore

- Unexplained hyperglycemia requires re-evaluation of insulin therapy
- Hyper or hypoglycemia occurring in the presence of intercurrent illness requires “management of sick days”
- For alterations in day to day activities, insulin must be altered accordingly
- Special advise is required in case of travel, fasting, change in activities and routine
- Diabetics on twice a day regimen require $\frac{2}{3}$ of their daily requirement of insulin in the morning and $\frac{1}{3}$ in the evening
- One third of the requirement for a dose is given as plain insulin and $\frac{2}{3}$ of the remaining for that dose as intermediate acting insulin
- On basal- bolus regimen, night time intermediate acting insulin may represent 30-50% of total daily insulin, 50-70% as rapid insulin divided to 3 or 4 pre-meal boluses.

Chapter 8

Complications of Diabetes mellitus – Acute

Complications of Diabetes mellitus – Acute

Dr. B.R. Giri MD.

Diabetes are prone to many acute complications, some of which are life threatening. These are medical emergencies and if these are not managed appropriately, it can result in mortality.

8.1. Severe life threatening complications or emergencies

- Hypoglycemic coma
- Diabetic Ketoacidosis with or without coma
- Hyperosmolar nonketotic coma
- Lactic acidosis

8.2 Mild complications

Mild complications are varied and are not so uncommon. These too require appropriate management as these can progress to more severe problems.

- Insulin oedema
- Blurred vision (presbiopia)
- Insulin allergy
- Acute neuropathy
- Insulin abscess
- Diabetic skin infections
- Diabetic genital infections.

8.3. Other Medical and surgical emergencies occurring in a diabetic

Diabetics are more prone to developing these complications. These are life threatening complications.

- Acute Myocardial Infarction
- Cerebrovascular accident
- Acute abdomen
- Diarrhoea and vomiting
- Trauma
- All other medical and surgical conditions as in non diabetic

8.4. Hypoglycaemic coma

Hypoglycaemic coma is the commonest emergency in a diabetic individual. The most common causes of hypoglycaemia are excess dosing of insulin or oral hypoglycaemic drugs, decreased carbohydrate intake and sudden increase in physical activity. Patients with hepatocellular disease and renal failure may also present in hypoglycaemia.

8.4.1 Symptoms and signs of hypoglycaemia

Adrenergic

- Headache, palpitation
- Confusion, Paraesthesia
- Hypothermia, Paralysis
- Seizures, Coma

Neuroglycopenic

- Sweating, Trembling,
- Looking pale
- Weakness, Hunger
- Lack of concentration
- Irritability/aggressive behavior

8.4.2. Stages of hypoglycemia

- Mild : No assistance required for recognition or treatment
- Moderate : Some assistance required for recognition and/or treatment
- Severe: Unable to recognise or treat

Treat all hypoglycemia immediately

8.4.3. Treating hypoglycemia

If hypoglycaemia is noticed, treat the patient immediately. Mild to moderate hypoglycaemia can be managed at the place of work or at home. However, if severe hypoglycaemia is suspected, move the patient to the nearest health facility for institution of its management immediately.

8.4.3.1. Mild Hypoglycemia

- Check blood glucose level if possible
- Give 15 grams of quickly absorbed carbohydrate to eat like glucose powder, sugar, fruit juice etc.
- Also give another 15 grams of slow acting carbohydrate to eat
- Check blood glucose level after 10 minutes
- Treat again if blood glucose level is <72 mg/dl or signs and symptoms of hypoglycaemia persist.
- Identify cause of hypoglycaemia and remove the cause.
- Is there a further risk of hypoglycaemia? If it is there, advice against it.

8.4.3.2. Moderate hypoglycemia

- Ensure safety, do not leave the individual alone
- Check blood glucose level if possible
- Give 15 grams of quickly absorbed carbohydrate like sugar, glucose powder, and fruit juice.
- Give another 15 grams of slowly absorbed carbohydrate like rice, biscuits etc.
- Check blood glucose level after 10 minutes
- Treat again if blood glucose level is <72 mg/dl or signs and symptoms persist
- Identify cause of hypoglycemia and correct cause
- Look for further risk of hypoglycaemia. If it is present, advise on its correction.

8.4.3.3. Severe Hypoglycaemia

Severe hypoglycemia can be life threatening. Energetic and prompt management must be instituted to prevent permanent brain damage.

- Check blood glucose level if possible
- Place the patient on side and clear airway
- Give glucagon if available
- Phone ambulance or medical officer. Patient may need IV glucose if he/she is drowsy, confused, has seizures or is unconscious
- Treat as mild hypoglycaemia when consciousness is regained
- Give at least 45 grams of slowly absorbed carbohydrate if glucagon has been used

Preventing Hypoglycemia

Hypoglycaemia can easily be prevented if the following measures are followed by individuals who take insulin or oral hypoglycemic agents.

- Always carry quickly absorbed carbohydrate
- Take injections, tablets, meals and snacks as recommended
- Plan for unusual exercise
- Do not drink alcohol without food
- Monitor blood glucose levels
- Know how to recognise and treat hypoglycaemia
- At the slightest symptom of hypoglycaemia, the individual must take easily absorbed carbohydrate immediately.

8.5. Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a medical emergency that is caused by inadequate insulin action which results in hyperglycemia, osmotic diuresis, lipolysis,

ketonaemia, and water and electrolyte losses. These metabolic changes lead to drowsiness and confusion, stupor, shock, coma or death, unless they are treated urgently. Mortality rates due to severe DKA and coma still remain high, varying from 5-10% in specialized centers and up to 25% in other hospitals.

8.5.1. Precipitating factors

Diabetic ketoacidosis is precipitated in persons taking insulin or other hypoglycaemic agents by following conditions.

- Inadequate insulin or omission of insulin in Type 1 Diabetes
- Diabetes patients having sudden severe stress like
 - Infections
 - Stroke
 - Myocardial infection
 - Trauma.

8.5.2 Clinical presentation

Diabetic ketoacidosis must be suspected in any patient either on insulin or other hypoglycaemic agents if they develop following manifestations.

- Exacerbation of thirst, polyuria and weakness.
- Dry skin, dry mucous membrane, sunken eyeballs due to dehydration
- Rapid respiration and air hunger, progressing to Kussmaul breathing in severe cases.
- Oliguria which follows initial phase of polyuria.
- Nausea, vomiting, weakness and malaise.
- Muscle aches, and severe abdominal pain especially in children.
- Hypotension and tachycardia with a rapid but weak pulse.
- Depression of the central nervous system, with headache, drowsiness, stupor and convulsion, followed by coma.

8.5.3. Diagnosis

Most careful history, clinical examination and simple biochemical investigations confirm the diagnosis.

8.5.3.1. Biochemical findings

Raised blood sugar levels are always present in DKA. However, blood sugar level does not correlate with severity of the illness. Diabetic ketoacidosis is seen even with a blood sugar level of 250 mg%. Ketone bodies are present in urine and also in plasma. Blood ketone levels are often raised by about 100 fold or more. Serum bicarbonate levels are low, (usually less than 15mEq/L) and blood pH is reduced. Serum protein, haemoglobin and haematocrit levels are raised due to dehydration. Leucocytosis is common and does not always indicate infection.

8.5.4. Principles of management

Following are the principles of management of diabetic ketoacidosis.

- Correction of dehydration.
- Maintenance of circulation
- Correction of acidosis
- Correction of electrolyte imbalance
- Correction of hyperglycemia
- General care of comatose patient
- Treatment of infection (if present)

It is of crucial importance that the most important causes of death in DKA are

- Before treatment is initiated
 - Cardiovascular collapse
 - Acidosis
- After 4- 8 hours of initiation of treatment
 - Cerebral edema due to rapid excess fluid infusion and rapid lowering of blood sugar
 - Hypokalaemia due to insulin induced influx of potassium into the cells

8.5.4.1. Fluid Management

Diabetic ketoacidosis have severe degree of dehydration. Rehydration is of first priority. This will avoid or correct cardiovascular collapse and prevent early death. Isotonic saline can be safely used in the following schedule :

- o 1 liter in the first half hour,
- o then 1 liter in one hr.+ Kcl 1 amp
- o then 1 liter in 2 hr, + Kcl 1 amp
- o then 1 liter in 4 hr,
- o then 1 liter 8 hourly or as clinical state demands.

If serum Na⁺ levels exceed 155 mEq/L, half normal saline should be infused. If half normal saline is not available, pass a NG tube and run equal volume of distilled water maintaining the calculated volume of fluid. In patients with cardiovascular disease or in the elderly, fluid replacement should be done with care, if possible, with central venous pressure monitoring. Once blood glucose levels have fallen to 250 mg%, 10% glucose should be infused 500ml every 4 hours.

8.5.4.2. Insulin Management

Insulin can be used either through continuous intravenous route or given intramuscularly depending upon available facilities, expertise and experience.

Intramuscular insulin

The patient is given 20 units (10-25 units) soluble insulin initially followed by

4-6 units hourly until blood glucose falls to 250 mg%, then 6 unit is given IM 2 hourly with 10% glucose (500 ml/4 hrs).

This is continued till the first meal when soluble insulin is given thrice daily (e.g. 12 units thrice daily) or the patient is put back on his usual pre-admission insulin regime.

There is no alternative to frequent blood glucose estimation for proper insulin dosing.

Continuous intravenous infusion of insulin

This is possible only in specialized centers where facilities for continuous insulin infusion and biochemical monitoring are available.

Bolus insulin is given at a rate of 0.1unit/kg weight followed by the following hourly regimen either through infusion set or through microdrip set.

Table 8.1:Insulin infusion rate

Spot blood sugar(capillary) mg/dl	Intravenous Insulin (Infusion pump) International Unit (IU)
< 140	Omit
141 to180	1 unit / hour
181 to 220	2 units/hour
221 to 260	3units/hour
>261	4 units/hour

Blood glucose must be monitored hourly, urine acetone two hourly, ABG and K+ 8 hourly. In most cases blood sugar fall by about 90 mg% per hour. When blood glucose falls to 250mg%, insulin infusion rate is decreased to 2-3 units/hour. In case of children under the age of 10 years 3 units/hour of insulin is sufficient.

When blood sugar level stabilizes, subcutaneous insulin can be begun as the patient is able to eat orally. Add hourly insulin requirement of the last six hours and multiply the sum by four, which is the daily insulin requirement of the patient.

Give 1/3 of daily requirement as plain insulin and other 2/3 as lente.

Intermediate acting insulin is given in two doses, 2/3 of the total pre-breakfast and the other 1/3 before dinner. Plain insulin is divided equally in three doses and given pre-breakfast, pre-lunch and pre-dinner to counter the post-meal blood glucose surge.

Give the first dose of fixed regimen but continue insulin through insulin pump for one more hour before finally discontinuing it.

Plain and Lente insulin must be mixed and instituted before breakfast and dinner. Premixed insulin is used in similar dosage and frequency. Dose adjustment of insulin is made every three to four days.

8.5.4.3. Management of Electrolytes

Dyselectrolytemia is an important cause of mortality in diabetes ketoacidosis. Management of electrolyte is another equally important aspect in the management of diabetic ketoacidosis.

Potassium

Hypokalaemia is a major cause of avoidable mortality in treatment of DKA. Replacement of potassium should therefore be started from the time of initiation of insulin therapy. Add potassium after 2 liters of fluid has been infused and when **diuresis occur**.

- ◆ Serum K⁺ is 6 mEq/lit: Do not add potassium
- ◆ Serum K⁺ 5-6 mEq/lit: add 10 mmol/hr of intravenous potassium
- ◆ Serum K⁺ 3-5 mEq/lit: 30mmol/hr.of intravenous potassium
- ◆ Serum K⁺ < 3 mEq/lit: 40 mmol/hr. of intravenous potassium

Add 30-40 mEq of K⁺ to a litre of intravenous fluid but not more than 30m Eq. per hour and not more than 120 mEq in 24 hours followed by oral potassium for a week.

Bicarbonate:

Bicarbonate therapy is generally not necessary when low dose insulin regime is followed.

However, if pH is less than 7.0, then 100mg sodium bicarbonate added with 20mmol potassium should be given in 45 to 60 minutes. Bicarbonate may be needed in painful hyperventilation.

Supportive measures and general care

Precipitating factor must be identified and dealt with like antibiotics for infection. Gastric aspiration must be done to relieve paralytic stomach and prevent aspiration. All other supportive measures must be instituted simultaneously.

8.6. Hyperosmolar non ketotic coma (HONK)

There is severe hyperglycemia (blood glucose>600mg %), plasma hyperosmolality, lack of ketoacidosis and severe dehydration. It occurs more commonly in older Type 2 diabetics. This is associated with a high mortality rate of 20 to 70%.

8.6.1. Clinical features

Long period of polyuria, polydipsia, vomiting and stopping of food and fluid intake, anorexia, confusion, drowsiness and coma are some features. There may be a variety of neurological deficits.

8.6.2. Precipitating factors

- Majority have underlying chronic illness of kidneys, liver, hypertension or stroke
- Patients may be on drugs that aggravate diabetes like diuretics, steroid etc.
- Uncontrolled diabetic state precipitated by infection, burn, myocardial infarction or stroke.
- Therapeutic measures in diabetic like peritoneal or haemodialysis, surgery etc.

8.6.3. Laboratory findings

There is marked hyperglycemia, plasma hyperosmolality in the presence of minimal or no ketosis and acidosis. Hypernatraemia is present in 50% of cases. Plasma bicarbonate may be moderately decreased due to renal acidosis or occasionally some lactic acidosis if the patient is in shock.

Plasma potassium tends to be normal or low, despite large deficit of total body potassium.

Table 8.2: Differentiating HONK from DKA

	DKA	HONK
Blood glucose	>14 mmol/L (252 mg/dl)	>33 mmol/L (594 mg/dl)
Ketones	Urine: mod - large Blood: > 3 mmol/L	Urine: neg - small Blood: <0.6 mmol/L
Osmolality	Increased - dehydrated	> 350m Osm/kg very dehydrated
Electrolytes	Low Na ⁺ Low HCO ₃ (< 15) K ⁺ Increased or decreased	High Na ⁺ High HCO ₃ (> 15)
Anion gap	> 10 mild > 12 mod-severe	< 12
PH	< 7.30	> 7.30

8.6.4. Treatment

Hyperosmolar non ketotic coma is a medical emergency with high mortality rate. This condition must be managed aggressively.

8.6.4.1. Fluid replacement

It is the first priority. Isotonic (0.9% saline) may be used initially while laboratory results are awaited. In hypernatraemic patients with plasma sodium more than 145mEq/L half normal saline should be used. In other patients normal saline can be continued. Rate of administration should be fairly rapid, 2 liters in first 2 hours followed by 1 liter every 2 hours until blood glucose reaches 250mg/dl when 5% glucose should be used. If half normal saline is not available, pass a nasogastric tube and feed same amount of plain water as normal saline keeping the ultimate fluid requirement to a balance. One can transfuse same volume of distilled water too. In elderly patients with cardiovascular disease fluid replacement should be carefully monitored.

8.6.4.2. Insulin

The patients are relatively sensitive to insulin, so a dose of soluble insulin half one would use in DKA, that is, 3 units hourly by continuous intravenous infusion, or 5 units intramuscularly hourly. When blood glucose falls to 250mg%, insulin is given intramuscularly every 4 to 5 hours.

8.6.4.3. Potassium

Potassium replacement is done as in DKA starting once diuresis has commenced, usually with the second liter of saline. In general 250 mEq are given in the first 24 hours. Oral potassium is then given for a week.

8.6.4.4. Other measures

Precipitating factors need recognition and adequate management.

Chapter 9

Complications of diabetes – Chronic

Complications of diabetes – Chronic

Dr.B.R. Giri MD.

Diabetes is a multisystem metabolic disorder. Chronic complications begin much before diabetes is detected. As diabetes result in damage of both large and small blood vessels, most organ system of body are vulnerable to chronic diabetic complications. Some patients present with complications for the first time.

9.1 Ocular complications

Each structure of ocular tissue and adnexa is vulnerable to this chronic disorder. Commonest involvement of eye is that of retina which can be devastating resulting ultimately in loss of vision.

- Diabetic Retinopathy
- Diabetic cataract
 - ♦ Early, Senile
 - ♦ True Diabetic (Snow Flake)
- Recurrent Iritis
- Infections

9.1.1. Risk factors of diabetic retinopathy

- Poor glycaemic control
- Long duration
- Hypertension
- Hypercholesterolaemia
- Nephropathy
- Pregnancy

9.1.2. Classification of diabetic retinopathy

- Non-Proliferative diabetic retinopathy
 - ♦ minimal, mild, moderate, severe
- Proliferative diabetic retinopathy
 - ♦ High-risk PDR, advanced PDR
- Macular oedema, clinically significant macular oedema

9.1.2.1. Mild to moderate Non Proliferative Diabetic Retinopathy

There are mild to moderate number of microaneurysms and haemorrhages. Hard and soft exudates may be present. This requires meticulous control of blood sugar, micro-photograph of the fundus for future reference and, follow up examination every 4 to 6 months.

9.1.2.2. Severe Non Proliferative Diabetic Retinopathy

A large number of microaneurysms are seen. However, no new vessel is seen. Vision is good unless maculopathy supervenes. This requires fluorescein angiography and photocoagulation.

9.1.2.3. Proliferative diabetic retinopathy (PDR)

New vessel formation and fibrous tissue proliferation occur in retina, disc and vitreous. Vitreous hemorrhage and retinal detachment result in severe loss of vision

9.1.2.3. Diabetic maculopathy

This is characterized by exudates, edema and haemorrhage at the macula. Vision is reduced severely in advanced stages of the disease. This requires treatment by photocoagulation.

The latest modality of treatment is vitrectomy and intravitreal triamniolone injection.

9.1.3. Other eye complications

9.1.2.3. Refractive error

This is a common eye complication in diabetes. Diabetics need to undergo frequent refractive error examination.

9.1.2.3. Lens

Risk of cataract formation is 204 times more in diabetics than in non-diabetic subjects. The risk of cataract increases by 15 to 20 times after the age of 40.

9.1.2.3. Vitreous

Due to neovascularization in retina, risk of haemorrhage and extension into the vitreous is high, resulting in uniocular blindness.

Other eye complications are orbito-rhinomucormicosis, xanthelesma, and decreased tear, paresis of extra ocular muscles, bells palsy, corneal ulcer, raised intraocular pressure, iritis and deposits of pigment in iris.

9.1.2.3. Therapy

Good control of blood sugar is of vital importance, to reverse ocular complications. Patients who have early eye complications require insulin supplementation.

9.1.4. Important to remember

- All diabetics must know of sight threatening diabetic eye complications
- Complete eye evaluation must be done at initial diagnosis of diabetes
- Yearly eye evaluation must be done if retinopathy is absent, otherwise six monthly eye evaluation is necessary
- Diabetic who is planning for pregnancy or is already pregnant must undergo complete eye evaluation every trimester
- Good glycemic control delays eye complications
- Timely detection and treatment of diabetes reduce but do not prevent development of decreased vision.
- It is the duration and not severity of diabetes that effect ocular tissues.
- No treatment modality reverses diabetic complications but halt or delay the progression.
- All patients 10-30 years of age with 5 or more years of diabetes or all diabetics diagnosed after 30 years of age should be evaluated by ophthalmologist.

9.2. Diabetic Neuropathy

Diabetic neuropathy is a common, disabling chronic complication of diabetes. Up to 50% of patients with diabetes having the disease for 20 to 25 years have neuropathy. The incidence and severity of neuropathy progresses with duration of diabetes.

Nerve function deteriorates due to pressure, ischaemia or various metabolic abnormalities.

The common etiology of neuropathy are as follows:

- Sorbitol accumulation in nerve cells and sheath
- Myoinositol depletion
- Microangiopathy

9.2.1. Classification of diabetic neuropathy

Diabetes results in progressive irreversible nerve damage. Damage to nerve can be varied. The commoner ones are as follows:

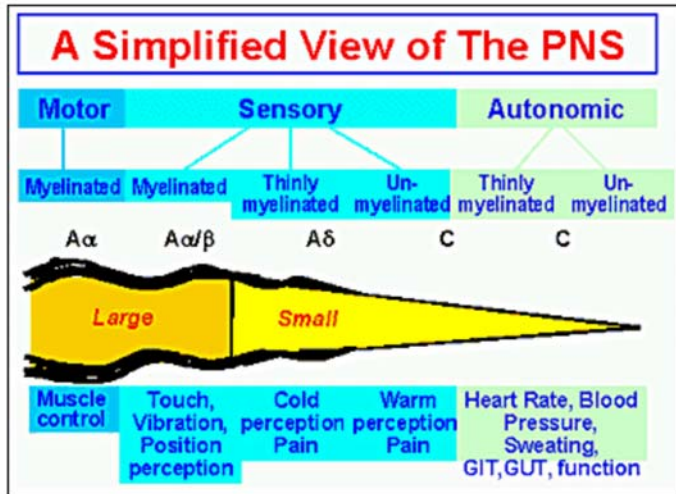
1. Diffuse symmetrical diabetic polyneuropathy
2. Small fiber neuropathy
3. Autonomic neuropathy

Diabetes also results in acute reversible neuropathy. They are as follows:

1. Femoral neuropathy
2. Cranial nerve palsy
3. Truncal and thoracic neuropathy

9.2.1.1. Distal Symmetrical Neuropathy

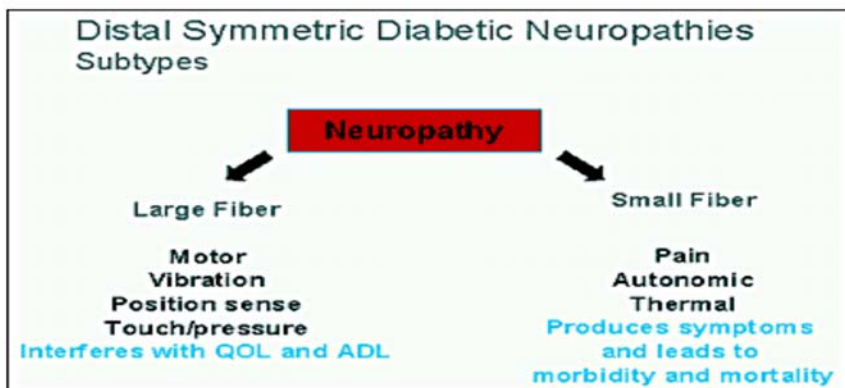
Distal symmetrical neuropathy is the commonest type of neuropathy, present in 40% of diabetics of 25 years duration.



Clinical features are paresthesias, pins and needles sensation of feet and hands, dull aching or lancinating pain, worse at night, burning sensation of sole, cutaneous hyperaesthesia, wide based gait, sense of numbness of feet, absent ankle jerk, impaired sensation to light touch (glove and stocking), vibration and position where large fiber involvement occur. In small fiber involvement, dull aching pain with impaired pain, touch and temperature sensation occur.

9.2.1.2. Autonomic neuropathy

This is associated with symmetrical sensory neuropathy. It can be asymptomatic or cause incapacitating disability. Majority of patients developing autonomic neuropathy die within five years of developing symptoms.



- **Cardiovascular**
 - o Postural hypotension:
It occurs when systolic BP falls by 30 mm Hg on change of posture.
It occurs on standing erect accompanied by weakness, dizziness, visual impairment and syncope.
 - o Painless myocardial infarction
 - o Sudden cardio-respiratory arrest may occur
- **Gastro intestinal**
 - o Dysphagia occur due to oesophageal atony.
 - o Gastroparesis resulting in delayed gastric emptying, nausea, vomiting and abdominal fullness occur which is relieved by metochlorpromide 10mg before each meal
 - o Nocturnal diarrhea, faecal incontinence
- **Genitourinary**
 - o Bladder dysfunction due to loss of bladder sensation occur resulting in unawareness of desire to micturate, absence of nocturia, poor urinary stream, incomplete urinary emptying, overflow incontinence. Urinary stasis predisposes to infection.
 - o Impotence occurs in 25 percent of male diabetics.
 - o Retrograde ejaculation is a cause of reduced fertility.
 - o Reduced vaginal lubrication and dyspareunia
- **Pseudomotor**
 - o Gustatory sweating: Profuse sweating occur while eating, precipitated by cheese and spices.
 - o Nocturnal sweating without hypoglycemia also occurs.
- **Respiratory**
 - o Impaired breathing control
 - o Sleep apnea
- **Vasomotor**
 - o Abnormalities like cold feet, dry feet
 - o Dependent edema .
 - o Bulla formation in the extremities

9.2.1.3. Hypoglycemic unawareness

There is denervation of sympathetic and parasympathetic nerves as well as hypothalamic dysfunction. There is impairment of counter regulatory hormones as well.

Patients with autonomic neuropathy are prone to hypoglycemia without being aware of it.

9.2.1.2. Rapidly reversible neuropathy

Newly diagnosed diabetics present with neuropathy which rapidly improve on glycemic control.

The nerves that are commonly involved in this condition are.

- Femoral neuropathy
- Cranial nerve palsy
- Truncal & thoracic neuropathy

9.2.1.5. Mononeuropathy and Multiple neuropathy

Mono neuropathy

There may be sudden wrist drop, foot drop or paralysis of one of the cranial nerves viz. 3rd, 4th, 6th or 7th. Third nerve is commonly affected. However, almost every peripheral nerve is affected by mononeuropathy, examples being radial, ulnar, median, etc. There is high degree of spontaneous recovery over several weeks when blood sugar is controlled.

Diabetic amyotrophy

Proximal motor neuropathy result in severe pain and paresthesia in the upper legs and weakness and muscle wasting of the quadriceps occur.

Radiculopathy

Diabetics may have severe pain along a dermatome. Symptoms simulate herpes zooster without skin lesion.

Diabetic neuropathic cachexia

It is common in elderly diabetics with marked weight loss, painful peripheral neuropathy and depression.

9.2.2. Management

Meticulous glycemic control delays neuropathic complications. Treatment of chronic diabetic neuropathy is not satisfactory

9.2.2.1. Drugs

- Amitriptyline 50-125 mg/day, starting with a low dose which is gradual increased.
- Fluphenazine 1 mg three times a day may be given where available.
- Imipramine 50 to 100 mg a day is an alternative.
- Desimipramine 75 mg at bed time
- Carbamazepine 400-1200mg in 2 divided doses
- Gabapentin 600-1800 mg in 3 divided doses
- Tramadol 50 mg 2-3 times a day
- Capsaicin 0.075 mg cream, to be applied locally 4 times a day

9.2.2.2. Local applicants

- o Lignocaine
- o Maxiletene
- o Capsaicin 0.075mg cream, apply locally 4 times a day is especially useful in burning feet syndrome

9.2.2.3. Non-pharmacological treatment

- Difficult to manage
- Leg exercises to increase venous return prior to stand up
- To sit for a few minutes before standing from a lying down position
- Supportive stocking should be applied while lying down and it must not be removed until returning to supine position.

9.3. Diabetic nephropathy

Diabetic nephropathy is one of the microvascular complications of diabetes, manifested by proteinuria, progressive rise in blood pressure and fall of GFR. Prevalence is more in Type 1 than Type 2 diabetes. It is a common cause of end stage renal failure. Diabetic nephropathy is associated with a variety of clinical syndrome including mild symptomatic proteinuria, nephritic syndrome, hypertension and progressive renal failure. Presence of microalbuminuria in a young diabetic is indicative of impending nephropathy. Tight control of blood sugar and use of ACE inhibitor may reverse microalbuminuria. Control of hypertension is very important once albuminuria develop to prevent progressive kidney damage.

9.3.1. Stages of Diabetic nephropathy

Diabetes nephropathy develops over a period of 10 to 20 years. It passes through several stages. At onset, kidneys are usually large with hyperfiltration.

Table 9.1: Stages in Diabetes Nephropathy

Stage	Glomerular filtration	Albuminuria	Blood pressure	Time course (Years after diagnosis)
Renal hyper-function	Elevated	Absent	Normal	At diagnosis
Microalbuminuria (incipient-Nephropathy)	Within normal range	30-300mg/day (within or above)	Rising	5-15
Macroalbuminuria or persisting proteinuria (Nethropathy)	Decreasing	>300mg/day	Increased	10-15
Renal failure	Diminished	Massive	Increased	15-20

9.3.2. Albuminuria

Screening of albuminuria is important in younger diabetics. It is a nonspecific test and common in hypertensive, following urinary tract infection, exercise and in congestive heart failure.

9.3.3 Guidelines for investigation

All patients detected diabetic at the first instant should have their renal function assessed. Urinary proteins, blood urea, creatinine and electrolytes should be checked. Those who have positive test for protein in routine test should have 24 hour urinary protein estimation done. In those who do not test positive for protein in routine test must undergo test for microalbumin.

9.3.4. Prophylaxis for diabetic nephropathy

- Primary prophylaxis: Control of glycaemia.
- Secondary prophylaxis: Control of blood pressure with ACE inhibitors and ARBs.
- Tertiary prophylaxis: Dietary protein restriction.

9.3.5. Management

9.3.5.1. Glycaemic control

Good glycaemic control reduces risk of diabetic nephropathy by 35 to 56 % in Type 1 diabetes.

Optimum glycaemic control must be done.

9.3.5.2. Blood pressure control

Blood pressure must be controlled very well. With the onset of microalbuminuria, antihypertensives must be started. ACE inhibitors are known to have renoprotective effect.

Target BP

1. Without microalbuminuria: 130/80 mm Hg.
2. With microalbuminuria : 120/75 mm Hg.

Verapamil or beta blocker also reduce microalbuminuria but less consistently. ACE inhibitor may be combined with Angiotensin Receptor blocker for maximum antiproteinuric effect. Thiazide diuretics may be used as first line antihypertensive.

9.3.5.3. Diet

Protein intake in excess should be avoided. It should be imposed early in the disease. Protein must be restricted to 0.5 to 0.75 mg/kg body weight. Proteins of high biological value must be encouraged. Fluid overload and hyperkalaemia must be checked and managed.

9.3.5.4. Hypoglycemic agents

- Long acting hypoglycaemic agents and metformin must be stopped
- Short acting sulphonyluria may be started viz. glipizide, gliclazide
- Short acting insulin controls sugar well in renal failure

9.3.6. Remember the following

- On screening albuminuria, if it is present, exclude other causes of microalbuminuria.
- Repeat yearly microalbuminuria, if negative.
- Screening for albuminuria : if positive by dip stick/heat coagulation test do quantitative estimation of 24 hours urinary albumin excretion
- Repeat at 3 monthly interval.
- If negative check for microalbuminuria.
- Renal function tests such as blood urea, creatinine and electrolytes must be done simultaneously.
- Motivate the patient about primary, secondary and tertiary prevention of diabetic nephropathy.
- Motivate the patient about glycemic control, blood pressure normalization, and inform of the precipitating illness aggravating the condition.
- Consider ACE inhibitor or ARBs, to slow the rate of progression. Protein restriction, phosphate lowering agent may have benefit in selected patients
- Avoid NSAIDs as they are nephrotoxic.

- In severe renal failure, patients need renal replacement therapy, either by hemodialysis or renal transplantation. The later gives the best quality of life.

9.4. Peripheral Vascular Disease

Atherosclerosis of arteries supplying the legs is the most common form of peripheral vascular disease. Atherosclerosis usually affects the large arteries down to the popliteal artery. It is a part of generalized atherosclerotic process which also affects the coronary and extra cranial arteries. Fifteen years mortality of a patient at presentation with claudication is 75% and 50% of death is due to cardiac events and another 15% due to extra cardiac vascular events. Other causes of chronic limb ischaemia are due to Burger's disease, popliteal entrapment, arteritis and vasospastic disease.

Areas of skin necrosis, often over pressure points occur in diabetic foot. Although cause of necrosis is due to proximal atherosclerosis, more commonly there is an additional element of microvascular diabetic angiopathy affecting the smaller vessels.

Diabetic sensory neuropathy often allows the lesion to become extensive before the patient seeks medical help. Principal difference in management is that amputation of individual toes or fore foot can often heal successfully if there is no proximal atherosclerosis. Such local amputations are inappropriate in non diabetic patients with pure proximal large vessel diseases. Major cause of death in patients with peripheral vascular disease is myocardial infarction. So it is important to reduce risk factors as far as possible.

9.4.1. Clinical Features

Progressive narrowing of arteries (supplying legs) produces typical symptoms of intermittent claudication (i.e. muscle pain on walking a certain distance, which is relieved by a few minutes of rest). Patients first become aware of symptoms when walking uphill or climbing stairs. Some patients may develop rest pain in affected limb. This is worse at night and patient may get temporary relief by allowing limb to hang over the side of bed outside bed clothes. Calf muscles are the most commonly affected muscles.

9.4.2. Risk factors for the development of atherosclerosis

Atherosclerosis develops over a period of time. Following are some factors that predispose an individual to developing atherosclerosis.

- Smoking
- Diabetes

- Hyperlipidaemia
- Hypertension.
- Ageing
- Male sex

9.4.3. Management

Most patients have mild claudication. It is necessary only to exclude any treatable underlying disease.

9.4.3.2. General

- Abstain from smoking
- Patient should be reassured that intermittent claudication may be uncomfortable but it is not harmful.
- Stop vasoconstrictor drugs e.g. beta blockers
- Maintain normal blood glucose in diabetic.
- Regular exercise increases collateral flow. The importance of regular exercise should be emphasized, as patient may anticipate pain and stop exercising before onset of claudication.
This is both psychologically and physiologically undesirable.
- Foot Care: Patients must examine their foot everyday to look for any redness, induration, injury, infection or ulcer.
- Drug therapy: Medication has little role in peripheral vascular disease, but vasodilators may be useful where there is substantial vasospastic component (Nifedipine 5-10 mg tid). Severe pain especially with neuropathic component may be helped by amitriptylline (25-50mg).
- Surgery: Only on severe disability, intractable pain, limb salvage.

9.4.3.2. Surgical options

- Percutaneous transluminal angioplasty (PTA) is the simplest catheter reopening procedure.
A guide wire is introduced percutaneously into the femoral artery and is directed under radiological guidance into the distal femoral arteries.
- Local fibrinolytic therapy is an alternative or an additional technique to PTA, particularly if there is a suggestion of recent thrombosis. Fibrinolytic agents are delivered through a catheter directly into the occlusion. A commonly used regimen is streptokinase, 6000 units per hour with repeat arteriography after 6 – 12 hours of treatment. If there is significant improvement, the treatment is continued for 24 – 48 hours with repeat arteriogram every 12 hours.
- Combination of PTA and Fibrinolytic therapy.
- Bypass graft
- Amputation where gangrene has set in and conservative measures are unsuccessful

9.5. Diabetic Foot Ulcers

Diabetes mellitus is one of the most debilitating disease that man faces. Diabetes is a disease of whole body. Multiple factors including neuropathy, angiopathy, immunodeficiency, hyperglycemia, nutritional status are in someway or other responsible for the devastating effects of diabetic foot infection.

Foot ulcer is the most common cause of hospitalization of diabetics. Up to 9 – 10 % diabetics develop chronic foot ulcer. Infection become more severe and more refractory to treatment in diabetic then in non-diabetic. Diabetic complications including vascular insufficiency, neuropathy and hyperglycemia contribute to severity of many infections. This is due to inadequate tissue perfusion, capillary and lymphatic damage and changes in bactericidal and chemotactic properties of phagocytes. Foot infection results in a relatively high rate of limb amputation and are associated with a poor long term prognosis for survival. They occur in patients who have had diabetes for many years, and remained hyperglycemic with inadequate treatment. They also develop other complications of diabetes mainly ophthalmic, renal and cardiac.

9.5.1. Predisposing causes of foot ulcer

Three major factors contribute to development of foot ulcer in diabetics.

- Peripheral arterial disease.
- Peripheral neuropathy, and
- Increased susceptibility to infection.

9.5.1.1. Peripheral Vascular insufficiency

Vascular insufficiency could be due to micro or macro angiopathy. Approximately 50% of diabetics have evidence of arterial disease 10 to 15 years after onset of diabetes mellitus.

Microangiopathy which occurs in retina and kidney also occur in toes. It is present in 88% of diabetics in comparison to 23% of non-diabetics. There is usually intimal thickening and basement membrane thickening which interferes with diffusion of nutrients.

Edema of lower limb which accompanies cardiac failure, chronic renal failure and edema due to infection aggravate arterial insufficiency.

Normal foot has rich collateral circulation. In a diabetic, multiple complete or partial occlusion of large, medium and small vessels can convert a part of foot dependent on only one vessel to develop necrosis especially when infection sets in.

9.5.1.2. Neuropathy

Neuropathy occur in diabetes of more than 10 to 15 years. Motor, sensory and sympathetic nerves are affected causing deformity, insensitive or partially sensitive foot and dry non sweating feet. All these cause callus formation leading to pressure necrosis. Insensitive feet are prone to injuries in various ways. Because of poor eye sight, they can injure toes while clipping nail or step on sharp objects. Pressure necrosis occur when external pressure exceed capillary pressure, for example when insensitive feet lie on bed for prolonged time or when a tight shoe is used. Autonomic neuropathy cause dry fissured skin that crack easily, opening up avenue for infection.

9.5.1.3. Susceptibility to infection

Hyperglycemia causes defective phagocytosis and also facilitates growth of bacteria that enter tissue.

Ketoacidosis delays migration of granulocyte to site of lesion and depress bactericidal and phagocytic functions of these cells. Antibody production to response of bacterial antigens is also diminished. Microangiopathy facilitates infection through decreased tissue perfusion and low oxygen level. It also impairs delivery of granulocyte, antibiotics and antibodies to the site of infection.

Infection can be asymptomatic fungal infection to severe limb threatening or life threatening disorder. A great majority of patients present late. The reasons are due to patients' unawareness of neuropathy and poor vision. At times, lack of awareness of referring physician of the severity of disease process result in devastations. Often primary care physician sees the tip of an iceberg – a small ulcer and a bid of pus - where as extensive soft tissue destruction, and even osteomyelitis have already occurred.

9.5.2. Management

A diabetic with aseptic foot needs emergency treatment. A complete diabetic work up including culture of pus from wound should be done. Large doses of broad spectrum antibiotics should be given till results of culture sensitivity are available, when it can be changed if necessary. Blood glucose should be controlled with regular insulin, and should be monitored frequently. Usually 6-12 hours of treatment is necessary to prepare the patient for surgery.

Surgery is indicated in all patients except those with superficial ulcers, which can be managed conservatively, or superficial cellulites that respond to rest and antibiotics.

The need for prompt surgical drainage, debridement, or amputation when such procedure is indicated, should be stressed. Unfortunately needless delay on the part of the patient or physicians often occur which result in spreading infection,

vascular thrombosis and proximal extension of the destructive process threatening patient's limb and even life.

When blood supply is adequate aggressive debridement of all necrotic tissue should be performed, without regard to subsequent reconstruction. Usually diabetic foot infections are deceptive of amount of devitalized tissue and are invariably more extensive than that is suggested by initial clinical examination. De-roofing of all cavities and careful handling of adjacent healthy tissue is a must. Rough handling of tissue can cause necrosis of wound margin. Use of all types of tissue irritant and detergent should be avoided. Normal saline should be preferred during dressing and debridement.

When severe sepsis is present and foot salvage does seem to be impossible, an early decision in favour of amputation can save life.

After debridement of a diabetic foot, wound must be reassessed on a daily basis. If pus is found on the dressing, an inadequately drained pocket should be suspected.

Steps in diabetes foot ulcer management

- Control of diabetes with insulin
- Control of infection with antibiotic
- Pressure elimination
- Anti-tetanus measures should be given
- Adequate nutrition
- Look for kidney and cardiac status
- Wound care, debridement and dressing
- Some form of anesthesia is required during manipulation of wound except in insensitive foot
- Diabetic foot will tolerate extensive incision
- Wide surgical incision and drainage of deep infection is almost always necessary and should be considered
- Diabetic foot is often deceptive. Patient may have minimum or no pain. Typical signs of infection may be absent in early stage. Extent of deep tissue necrosis is often greater than that of clinical external appearance
- Excision of all dead tissue is a must
- Daily careful wound examination and debridement should be done.
- No corrosive or detergent should be used in the wound. Diluted H₂O₂ and diluted iodine (non irritant) can be used in gross infection; otherwise normal saline wash is the best with normal saline soaked gauze dressing, which can be changed 2 to 3 times daily.

9.5.3. Some practical tips

- History of diabetes treatment, glycemic control, self care and other diabetes related complication must be taken.

Look for:

- ♦ Full thickness ulcer
- ♦ Deep ulcer
- ♦ Ulcer to bone and osteomyelites
- ♦ Wet or dry gangrene
- ♦ In extensive gangrene, foot salvage is not possible

Signs of vascular insufficiency:

- ♦ Diminished or absent pulse
 - ♦ Loss of hair in the fore foot toes
 - ♦ Cornification of nails
 - ♦ Atrophic skin and subcutaneous tissue
 - ♦ Decreased skin temperature
 - ♦ Marked pallor on elevation
 - ♦ Venous filling time > 20 sec
 - ♦ Capillary filling time of finger tip > 3 sec
- All diabetics should examine their lower extremities for redness, wound, infection etc.
 - Periodic examination of vascularity and neuropathy of lower limbs must be done.
 - ♦ Palpate dorsalis pedis, posterior tibialis, popliteal and femoral arteries of both lower extremities at every visit.
 - ♦ Inspect skin color, temperature, skin texture.
 - ♦ Identify any ulcer, blister thoroughly.
 - Complications should be explained in easy language. Daily self foot examination should be taught.
 - Avoid extreme temperature.
 - Foot ware should be oversize. High heel shoes should be avoided by ladies.

Chapter 10

Elderly and Diabetes

Elderly and Diabetes

Dr.B.R. Giri MD.

Glucose tolerance deteriorates with age. Diabetes mellitus and its complications are important health problems in elderly. It is an increasing problem with average life expectancy on a rise. Post prandial blood sugar rises by 10 mg % per decade after 50 years of age. Macrovascular disease is higher in elderly diabetes. Most elderly diabetes is Type 2. Pathogenesis of elderly diabetes is same as for other patients. Other age related factors like sedentary life style, increased adiposity, coexistent medical conditions, and concomitant use of multiple glucose intolerant drugs also contribute to the development of hyperglycemia.

10.1. Insulin Secretion

Glucose stimulated insulin secretion is blunted with increasing age. There is reduced sensitivity of B-cells to glucose stimuli.

10.2. Insulin Resistance

Primary cause of deterioration in glucose in advancing age is tissue unresponsiveness to insulin.

Reduced physical activity, excess calorie and carbohydrate intake may secondarily induce and aggravate insulin resistance.

10.3. Clinical Features

Classical symptoms of polydipsia, polyphagia, polyuria are less common in elderly. Non-specific symptoms like fatigue, pruritus vulvae, incontinence, weight loss may be some features at presentation. Many patients may be detected on pre-operative screening. Some patients present with cataract, IHD or hypertension.

10.4. Chronic complications

10.4.1. Microangiopathy

10.4.1.1. Retinopathy

Diabetic retinopathy in general and maculopathy in particular are typically important problems of elderly diabetics. Prevalence of retinopathy (as of diabetes) rises with age. Maculopathy accounts for the majority of cases with visual loss. Photocoagulation is very effective in preservation of sight in this condition.

10.4.1.2. Maculopathy

It is identified by the presence of hard exudates, visual acuity less than 6/9 or a ring of hard exudates with a centrally visible vascular anomaly lying within one disc diameter of the fovea. Cataract, macular degeneration and glaucoma are common in elderly diabetic population.

10.4.1.3. Neuropathy

Absent ankle jerk and reduced vibration sense are common in non-diabetic elderly. Diabetic proximal motor neuropathy (Diabetic Amyotrophy) is common in elderly. There is asymmetric weakness of pelvic girdle and thigh muscles, with little sensory changes. It may be associated with excruciating pain over the limbs and marked loss of weight. Active physiotherapy and good glycaemic control ameliorates the problem in about 6 to 12 months. Autonomic neuropathy is equally common and may present as postural hypotension, hypoglycemic unawareness, gastric and urogenital abnormalities and impotence.

10.4.1.3. Diabetic Foot

Elderly diabetics are unable to see their feet because of poor eyesight, unable to feel them because of sensory loss and unable to bend down to touch them because of arthritis. About 20% of the diabetic admissions are for diabetic foot problems. Education aimed at preventive foot care could dramatically reduce amputation rate. Visually handicapped elderly diabetics with peripheral and autonomic neuropathy and peripheral atherosclerotic vascular disease are highly prone to diabetic foot symptom. Recurrent foot ulcers are common.

10.4.2. Macroangiopathy

Mortality due to cardiovascular complications is increased in elderly diabetics and in those with impaired glucose tolerance. Combination of aging with diabetes exposes these subjects to increased risk of atherosclerosis. Many aged may present with macrovascular changes. Older individuals are prone to hypertension and dyslipidaemia and thus the stage is set for the cardiac, cerebral and peripheral vascular disease. Obesity, sedentary life style and smoking may also contribute to morbidity.

10.4.3. Management

Exercise, diet, oral hypoglycemic agents and insulin are the modalities of therapy in elderly diabetics.

Emphasis on diet therapy is total caloric restriction. Total caloric restriction can be effectively emphasized by saying, “eat half of what you used to” in

obese diabetics. Individual food faddists must be respected and altered a little. Due concessions must be given for coexistent oral problems due to loss of teeth and taste. Second generation sulphonyluria (Glibenclamide) exhibit fewer drug interactions due to their non-ionic binding and their hypoglycemic potential.

Biguanides especially Metformin is a safe alternative for overweight diabetics. Renal impairment and cardiac failure are common in old age and caution is needed before prescribing biguanides as these predispose to lactic acidosis.

Persistent symptoms, ketonuria or continual weight loss while on maximum safe dose of oral agents are indications to introduce insulin. Rarely may they require complex split and mixed regime of insulin but majority of insulin requiring diabetics need to be given a single daily dose of intermediate acting insulin in the morning. If fasting hyperglycemia persists on this regime, some may require small quantities of intermediate acting insulin in the evening. Compliance with insulin regimens is usually good among the elderly.

10.4.4. Monitoring Control

Urine glucose testing is unreliable because of raised renal threshold for glucose in the elderly.

Hence, blood glucose monitoring at health facilities is the best way of monitoring diabetes control.

Home monitoring of blood glucose is encouraged. Periodic examination of HbA1C gives the degree of blood sugar control over a period of 2 to 3 months.

10.5. Conclusion

Hyperglycemia in elderly is an important health care problem. About 10% of persons > 60 years of age have diabetes and this will increase by another 10% for every decade. Mild degree of glucose intolerance for prolonged period has increased morbidity.

Elderly are vulnerable to various disease conditions. Diabetes and its complications add up to the already disease burdened population. Hence it is crucial to look for occurrence of diabetes and follow measures to delay its occurrence and prevent their complications.

Chapter 11

Diabetes Mellitus and Surgery

Diabetes Mellitus and Surgery

Dr. B.R. Giri MD.

With advancement in the management of all types of diabetes, life expectancy of diabetic has increased significantly. Patients with Type 2 Diabetes are nowadays expected to have near normal longevity. This increased life expectancy together with modern advances in medical and surgical therapies mean that a diabetic individual has an even greater chance of requiring surgery during life time. Thus health care team needs to be aware of metabolic problems that may arise during surgery. The elevation of counter regulatory hormones, associated suppression of insulin secretion, excessive lipolysis and ketogenesis that can all occur during surgery can have particularly deleterious effects on patient with diabetes. In addition complication of diabetes such as micro and macroangiopathy, nephropathy, neuropathy etc. may enhance morbidity and mortality of anesthesia in surgery.

If proper attention is not paid to keeping the plasma glucose level within an acceptable range in the preoperative period:

- The patient, especially with Type 1 Diabetes, may go into ketosis and acidemia and/or
- May be susceptible to electrolyte abnormalities and volume depletion from osmotic diuresis.

There is data indicating impaired wound strength and wound healing with high plasma glucose levels. Leukocyte functions of chemotaxis, opsonisation and phagocytosis are also affected by hyperglycemia.

11.1. Aims of Therapy

Unrecognized hypoglycemia in anesthetized patients may have serious consequences. So, a very “tight” intra-operative control of glucose level is unwise. During the peri-operative period not only should the chances of developing hypoglycemia be reduced, but also a simultaneous effort should be made to avoid hyperglycemia, undue protein catabolism and electrolyte disturbances.

Attention must also be paid to optimize cardiovascular status, reducing risk of infection, improving wound healing and circumventing problems due to long term complications of diabetes.

Modern inhalation anesthetics have relatively little effect on metabolism compared to the stress of surgery. Stabilized glycaemic state, full cardiovascular assessment including ECG, Serum creatinine and electrolytes measurement,

urine culture, the elimination of other sources of infection i.e. skin, dental etc. and careful examination for neuropathy are prerequisites for all elective surgery in diabetic.

In elective surgical procedure satisfactory preoperative glycaemic control (two hours after breakfast blood glucose level less than 199mg%) should be achieved either using short acting sulphonylurias or soluble insulin depending on type of patient and type of surgery to be done. The use of Biguanides or long acting sulphonylurias is not recommended since the first can induce lactic acidosis and the second can cause delayed hypoglycemia.

11.2. Preoperative Management

11.2.1. Type 1 Diabetes

All Type 1 diabetes patients need insulin during pre, per and post operative period. The glucose values achieved will depend on targets set. Best recommended goal ranges between from 78-178mg%.

Blood sugar monitoring is done every 2-4 hour by glucose strip and insulin dosage adjusted accordingly.

The addition of potassium to insulin is reported to prevent major excursions in the plasma potassium level. It can be concluded that for Type 1 diabetes patients undergoing major surgery GIK (glucose/insulin/potassium) regimen or a simple variant thereof is the treatment of choice to obtain safe and reasonable glycaemic control during surgery.

11.2.2. Type 2 Diabetes

Patients requiring minor surgery with reasonable glycaemic control do not require insulin. It should be emphasized however, that nearly all protocols depend on rapid blood glucose estimation. Most centers now use glucose oxidase dry test strip technology for this purpose.

11.2.2. Emergency surgery

In case of emergency surgery, metabolic status of patient should be rapidly assessed as ketoacidosis may coexist and glycaemic control is likely to be poor. Standard therapy for DKA should be started and surgery should be delayed for 2-3 hours until there is a metabolic improvement. GIK should be used pre-operatively in all cases, taking into account the increased insulin requirement in sepsis.

In Type 2 diabetes, GIK is continued until first food is eaten, at which time their

usual therapy can be reinstituted, keeping in mind that patient might need increased doses to counteract catabolic effect of surgery. If post operative period is complicated by infection or any other problem there will certainly be an extra demand for insulin.

11.2.2. Suggested protocol

- a) Unrecognized hypoglycemia in an anesthetized patient may have serious consequences and very “tight” intraoperative control of glucose level is unwise.
- b) The only satisfactory way of keeping an eye on the blood glucose level is by repeated estimation. This can be done using glucose oxidase dry strip.
- c) In all patients requiring elective surgery, pre-operative glycaemic control should be reasonable i.e. 2 hours after breakfast blood glucose level should not be more than 199 mg%.
- d) A thorough preoperative check is essential to exclude cardiovascular, renal and neurological problems.
- e) Because of risk of inducing lactic acidosis, biguanides are not used preoperatively. Similarly use of the long acting sulphonylurias such as Glibenclamide preoperatively is also not recommended for fear of inducing hypoglycemia. Gliclazide or Glipizide are the preferred oral hypoglycemic agent for preoperative blood glucose control wherever available.
- f) If preoperative blood glucose is not controlled with maximum recommended dose of oral hypoglycemic agent, then blood glucose should be controlled preoperatively using a short acting insulin.
- g) Diabetic patients, unless there is a pressing reason, should be put first on the operation theatre list to minimize the effect of prolonged fasting and dehydration.
- h) If possible, choice of anesthesia is either local or regional (such as spinal), this is not because general anesthesia is more stressful but because with local and regional anesthesia, it is possible to resume oral feeding quickly and also allows one to resume usual antidiabetic therapy as quickly as possible.
- i) If insulin is required, it is mainly as a glucose/insulin/potassium (GIK) infusion. This regime is somewhat inflexible i.e. it is not possible to quickly alter the insulin dosages without also altering the rate of glucose infusion. However, it is safe and it does not put the patient at risk of developing hypoglycemia.

11.2.3. Management of Type 1 Diabetes Mellitus and IRDM (Insulin Requiring Diabetes Mellitus During Elective Surgery).

These patients are usually admitted 48-72 hours preoperatively to make sure that they have satisfactory glycaemic control and to carry out preoperative investigations. If control is not satisfactory, operation is delayed until satisfactory control has been achieved. The use of long acting insulin is not encouraged preoperatively and all patients are converted to either intermediate acting or short acting insulin. Subsequent management on the day of the operation is as follow.

1. The patient fasts for about eight hours preoperatively and does not receive his morning dose of insulin.
2. Dry strip glucose estimate is carried out and if it is more than 200mg% then the operation is postponed.
3. It is advisable to also estimate the serum potassium level.
4. A GIK infusion is started at least an hour prior to the operation. If the K⁺ is known to be about or 5mmol/l or more, then K⁺ is omitted from the infusion regime.
5. Post-operatively blood glucose estimation is carried out 2-6 hourly, and insulin dose is adjusted accordingly. K⁺ estimation, if possible, should be carried out 6 hourly and infusion rate adjusted accordingly. The GIK regimen is continued until the consumption of the first meal after which subcutaneous insulin could be restarted, keeping in mind that stress effect of surgery might continue in the post operative period which may increase insulin requirement.
6. For minor operations this protocol is modified. Morning dose of insulin is omitted.

Immediate preoperative blood glucose is checked and if it is below 199mg%, the operation is carried out without any insulin cover. As soon as possible after operation, breakfast along with the patients' usual insulin is given. If blood glucose is found to be above 199mg%, or if the operation takes an unexpectedly long time the patient is given GIK regime and normal diet and insulin is started as soon as possible after the operation is over.

11.2.4. Initial set up of the GIK regime

To a bag of 500 ml of 5% dextrose solution 1gm of KCL solution is added. Short acting insulin is then added to this bag according to patients' blood glucose level using the following rough guide.

Table 11.1 : GIK Set up

Blood glucose	Insulin
<108mg%	No insulin
104-162%	6 unit
163-198mg%	8 unit
199-234%	10 unit
235-306%	12 unit

This mixture is then given intravenously at a rate of 100ml/hr. The volume infused is taken into account with the total volume of fluid infused and extra fluid is given as per requirement of the situation.

Blood glucose is checked 2 hours later and dose of insulin is adjusted accordingly using the above guide. If at any point blood glucose exceeds 306mg% then subcutaneous soluble insulin is added on top of the IV insulin. Four units of insulin is given subcutaneously if the blood glucose level is between 306-378mg/ and 8 units subcutaneously if the blood glucose is between 379-450mg%.

Potassium level is checked every 6-8 hours and if it goes above 5mmol/l, KCL is omitted from the next bag. If on the other hand it falls below 3 mmol/l an extra 1 gm of KCL is added to the next bag. If there are no facilities for checking serum potassium level, 1gm of KCL is added to alternate bag of 500 ml. of 5% dextrose solution.

Infusion regime outlined above is recommended in well controlled, uncomplicated diabetic patients.

For insulin resistant cases, dose of insulin needs to be increased. Insulin dosage is calculated following the rule of thumb mentioned below.

Obesity – 0.3 – 0.4 units per 1gm of glucose infusion + 7.5 - 10 units.
Liver disease – 0.5 – 0. unit per 1gm of glucose infusion + 12.5 - 15 units.
Severe infection – 0.5 – 0.8 units per 1 gm of glucose infusion + 12.5 - 20 units.
Steroid therapy – 0.5 – 0.6 units per 1gm of glucose infusion + 125 - 25 units.

500ml of 5% dextrose contain 25m glucose

500ml of 10% dextrose contain 50g glucose

500ml of 50% dextrose contain 250g glucose.

11.2.4. Type 2 Diabetes

11.2.4.1. Diet Control

If glycemic control is satisfactory, these patients are treated almost as though they are nondiabetic for the purpose of perioperative management. However, repeated blood glucose estimation should be carried out. If, during perioperative period glycaemic control gets out of hand GIK regime should be instituted promptly to gain satisfactory control.

11.2.4.2. Minor Operation

On the morning of operation, oral hypoglycemic agents are omitted and blood glucose is estimated. If blood glucose is satisfactory, operation is carried out and as soon as possible after operation, the patient is given food and first dose of oral hypoglycemic agent.

11.2.4.3. Major Operations

In the morning of operation, oral hypoglycemic agent is omitted and blood glucose level is estimated. If blood glucose level is satisfactory, GIK regime is started and operation is carried out under cover of GIK regime which is continued to immediate post operative period. When the patient is well enough to take orally, s/he is given SC insulin twice or three times daily, usually for a few days. Once insulin requirement of patient has come down to a reasonable level s/he is switched to oral hypoglycemic agent using the rule of thumb that 20 units of insulin is equivalent to 5mg of the Glibenclamide.

11.2.4.4. Emergency surgery

The operation is postponed until patient has been assessed inclusive of blood biochemistry, ketone bodies and glucose level. If there is derangement of any of these parameters, appropriate corrections are made by using GIK regime supplemented by other steps. Correction of ketoacidosis, dehydration, hyperkalemia etc. is more important than the actual blood glucose level prior to surgery. Once these have been corrected the patient can be safely subjected to surgery under cover of GIK regime which is of course continued in the post operative period.

11.3. Conclusion

Thorough assessment in the preoperative period is as important as pre and post operative management of a diabetic patient. There is no justification in carrying out an elective operation on a patient with poor glycaemic control. A few days of postponement to achieve satisfactory glycemic control will be richly rewarded by a smooth post operative period.

Chapter 12

Hypertension in Diabetes Mellitus

Hypertension in Diabetes Mellitus

Dr. B.R. Giri MD.

12.1 Introduction

Hypertension is a common problem in diabetic patients. The prevalence of hypertension in diabetic population is 1.5 to 3 times that in non-diabetic population. It is estimated that 30-75% of diabetic complication can be attributed to hypertension which is twice as common in diabetic as non-diabetic population. However, secondary causes of hypertension should also be excluded. Type 2 diabetes patients often have hypertension at presentation. Type 2 patients with hypertension frequently share risk factors like obesity, visceral adiposity and insulin resistance. Isolated systolic hypertension is common in Type 2 diabetes. The co-existence of diabetes and hypertension result in multiplication of macrovascular and microvascular complications. Macrovascular complications are responsible for majority of deaths in diabetes.

Classification and Management of Hypertension (JNC7)

Table 12.1 : Blood pressure of adults > 18 years of age

BP Classification	SBP mm Hg	DBP mm Hg	Life style Modification	Initial Drug therapy	
				Without compelling indication	With compelling indication(Table 2)
Normal	<120	<80	Encourage		
Prehypertension	120 to 139	80 - 90	Encourage	Antihypertensive not indicated	Drugs for compelling* indications
Stage 1 Hypertension	140-159	90-99	Encourage	Thiazides, may consider,ACEI,ARB, BB,CCB, a combination	Drugs for compelling indications. Other antihypertensive, diuretics, ACEI,ARB,BB, CCB,etc. as needed
Stage 2 Hypertension	>160	>100	Encourage		

JNC: Joint National Committee

* : BP goal in diabetes and chronic kidney disease <130/80 mm Hg

ACEI: Angiotensin 1 Inhibitor

ARB: Angiotensin Receptor Blocker

BB: Beta Blocker

CCB: Calcium Channel Blocker

Table 12.2 : Guidelines for compelling indications for individual drug classes

Compelling indications	Recommended Drugs					
	Diuretic	Beta Blocker	ACE1 Inhibitor	Angiotensin Receptor Blocker	Calcium Channel Blocker	Aldosterone Antagonist
Heart Failure Post Myocardial	*	*	*	*		*
Infarction High coronary		*	*			*
Disease risk	*	*	*		*	
Diabetes	*	*	*	*	*	*
Chronic Kidney Disease			*	*		
Recurrent stroke prevention		*	*			

Compelling indications for antihypertensive drugs are based on benefits from outcome studies and existing clinical guidelines

The higher reading (systolic and diastolic) should be selected to classify an individual's blood pressure status. Goal of therapy in diabetic hypertensive patients is to prevent death and disability with least disturbance in quality of life.

It is recommended that blood pressure for non pregnant diabetic patient is reduced and maintained at BP<130mm Hg systolic and <85mmHg diastolic. Blood pressure should be lowered even further if it is well tolerated.

12.2. Diagnosis of Hypertension

- With systolic BP >210 mmHg or diastolic BP >120 mmHG the diagnosis of hypertension can be made at first visit.
- In absence of very high BP, multiple readings on three occasions should be taken. Patients should rest for 5 minutes before BP is taken. Sitting BP usually is adequate. Arm should be at heart level.
- For patients who are over the age 65, diabetic or receiving

antihypertensive drug, postural change by taking readings immediately and 2 minutes after patient sits or stands should be taken.

- No caffeine or smoking before recording BP is allowed.
- Cuff size should be adequate; the blood pressure cuff should encircle and cover 2/3rd of circumference of arm. If bladder is small, false reading will be obtained.
- Initially, readings in both arms should be taken and if BP differs the higher reading should be recorded.
- Korotkoff phase V (disappearance of sound) is taken as diastolic blood pressure in adults whereas in children, phase IV (muffling) is considered.
- If Korotkoff sounds are weak, have the patient rise arm, open and close hand 5 to 10 times after which bladder is inflated quickly.
- Aneroid BP instrument should be calibrated every 6 month against a mercury BP machine.

12.3 Management of Hypertension in Diabetes

12.3.1 Treatment goal

Several trials on hypertension has shown direct relationship between systolic and diastolic blood pressure independently and cardiovascular events and mortality. Target blood pressure is defined as below 130/80 mm Hg in patients with hypertension and diabetes, or renal disorders.

The goal of treating high BP is to prevent death and disability without causing disturbance to quality of life. Treating SBP and DBP below 140/90 mm Hg is associated with decreased cardiovascular diseases and its complications.

Treatment is non-pharmacological and pharmacological.

12.3.1.1. Non-pharmacological treatment of hypertension

Lifestyle modifications

Life style modification is the fundamental requirement for management of diabetic hypertensive subjects. Pharmacological treatment for control of hypertension should be adhered for lifetime. Such patients should be educated at every available opportunity. Non pharmacological therapy alone is continued upto 3 months in prehypertension and stage1 hypertension, which generally controls high blood pressure.

Physical activity

Obesity is highly prevalent in Type 2 diabetes. Patients with diabetes and hypertension should do moderate aerobic exercise (isotonic) 60 minutes each

time, 7 days in a week. Exercise improves glycemic control (by improving insulin sensitivity) reduce and maintain body weight, improve physical capacity, improve lipid profile by decreasing plasma triglyceride, VLDL and LDL cholesterol level and increasing HDL cholesterol. Studies have shown that blood pressure falls invariably after 4 weeks of regular exercise for 30-45 minutes 3 to 4 times in a week.

Food

Low fat and high carbohydrate diet generally reduce risk of coronary heart disease but high carbohydrate diet can increase blood glucose level. Therefore, high carbohydrate may be avoided. Monosaturated fat is preferred to polysaturated. Vegetarians have lower blood pressure than non vegetarians, which probably is due to content of vegetable. High fibre diet also reduces postprandial rise of glucose. Consume diet rich in fruit, high in vegetable and low fat dairy products.

Minerals

Sodium retention is responsible for causation of hypertension. Most Type 2 diabetes patients with hypertension are sodium sensitive. Sodium restriction clearly reduces blood pressure. Hence, a sodium intake of less than 2.3g sodium or 5.8g of sodium chloride is advocated.

Smoking

Smoking raises blood pressure acutely but chronic smoking is not associated with higher blood pressure. Individuals with hypertension and diabetes should be strongly advised to avoid smoking as it is the most effective way to reduce cardiovascular risk.

Alcohol

Limit consumption of alcohol to no more than 2 units a day in men and one unit a day in women. Consumption of larger amount of alcohol is associated with a higher prevalence of hypertension and cause resistance to antihypertensive therapy.

Obesity

Obesity is prevalent in Type 2 diabetes. It is much more common in Type 2 diabetes who is hypertensive. Weight loss result in reduction of blood pressure in obese hypertensive. A target BMI of 18.5 to 24.9 must be maintained. BMI of $> 30 \text{ kg/m}^2$ is a risk factor for development of hypertension and CVD.

The Adult Treatment Panel III guideline for cholesterol management defines **metabolic syndrome** as the presence of three or more of the following conditions:

- Abdominal obesity (waist circumference > 40 inches for men and

>35 inches for women)

- Glucose intolerance (fasting sugar >110 mg/dl.),
- BP > 130/85 mm Hg,
- Triglyceride > 150mg/dl, and
- Low HDL (men < 40 mg/dl or women < 50 mg/dl)

Intensive lifestyle modification must be pursued in persons having metabolic syndrome. These individuals are highly prone to develop CAD and Type 2 Diabetes.

12.3.1.2. Pharmacological treatment of hypertension

In pre-hypertension, patients must be subjected to life style modification. This alone is adequate to control blood pressure of the individual. In stage I hypertension, life style modification and non-pharmacologic treatment may be continued for 3 months before starting drug therapy. In more severe form of hypertension, drug therapy is started at the time of diagnosis. Following classes of antihypertensive drugs can be started as monotherapy. Each class has its own advantage.

Beta Blockers

Those that block both B1 and B2 receptors are called non-cardioselective and include propranolol, timolol and nadolol. Those that block B1 receptors are cardioselective and include atenolol and metoprolol.

In addition to their antihypertensive effect B blockers are useful for treating IHD, various arrhythmias, noncardiac disease like migraine and essential tremor. Betablockers have been shown to reduce cardiovascular morbidity and mortality. They are the only class of drugs which prevent a second myocardial infarction and sudden death.

Beta blockers have some adverse effects on glycemic control, lipid level and peripheral blood flow. Erectile dysfunction, fatigue, cold extremities, bronchospasm in patients with underlying pulmonary disease, worsening of chronic heart failure, depression and disturbed sleep may occur with B blockers. B blockers may cause increase in blood glucose level, decreasing glucose stimulated insulin release by blocking B1 receptor in pancreas. Cardio selective agents have less impact on glycemic control and rise in blood glucose is very much minimal.

The most consistent effect of B blockers on lipid is an increase in serum triglyceride. A 10 – 15% decrease in HDL cholesterol is also noted.

Thiazide Diuretics (Hydrochlorthiazide)

Thiazide diuretics cause altered carbohydrate and lipid metabolism, hyperinsulinemia, hypokalemia, hypomagnesemia, hyperuricemia and ventricular ectopics. However, these side effects are very minimal at usual doses. Thiazide reduces plasma volume and it is established that plasma volume expansion is one of the pathogenic mechanism involved in causation of hypertension in diabetes. Excessive reduction in plasma volume may cause postural hypotension. Thiazides are particularly recommended in hypertension in elderly. Thiazide diuretics cause more sexual dysfunction than Beta blockers.

ACE inhibitors (Enalapril)

These are the most promising drugs in hypertension with diabetes. Studies comparing the efficacy of ACE inhibitors with Hydrochlorthiazide, Beta blocker and Calcium channel blockers show equivalent blood pressure lowering effect. Unlike other antihypertensive drugs ACE inhibitors increase insulin sensitivity and improve glycemic control. ACE inhibitors have been demonstrated to reduce microalbuminuria and nephropathy in normotensive and hypertensive patients. It improves insulin sensitivity, thereby improving glycemic control. The drug is also helpful in heart failure. ACE inhibitor should not be used in renal artery stenosis. Cough sometimes is a troubling side effect. Skin rash and angioedema can occur in rare cases. Postural hypotension is unusual unless the patient is volume depleted.

Angiotensin Receptor Blocker (Losartan)

These are one of the newer additions of antihypertensive drugs. These have effects similar to ACE1 inhibitors. These reduces proteinuria and have additive effect over ACE1 inhibitors.

Calcium Channel Blockers (Nifedepine)

This is an effective antihypertensive agent which is also helpful in patients with IHD. This has no adverse effect on lipid or blood glucose level. Pedal edema, constipation, headache and flushing may occur. Postural hypotension and sexual dysfunction is rare.

Alpha-receptor blocker

Prazocin has a very good blood pressure lowering effect. However, it can result in postural hypotension, especially in patients having autonomic neuropathy. This has beneficial effect on lipid and improves insulin sensitivity.

Other antihypertensive

Methyldopa is safe in pregnancy. Loop diuretics should replace thiazides if serum creatinine is more than 2 mg%. Potassium sparing diuretics should be used with caution because of the risk of hyperkalemia.

12.4. Autonomic Dysfunction and Hypertension

Diabetic patients with hypertension with autonomic dysfunction have a peculiar problem of supine hypertension and upright hypotension. These patients need to use pressure graded elastic support in the lower extremities, take increased amount of salt, fludrocortisone and NSAID. Supine hypertension must be treated by elevating the head end of bed, eating small meal at bed time and low dose calcium channel blocker.

12.5. Drug Selection in Hypertension in Diabetics

JNC 7 recommendations states that in order to achieve target blood pressure of < 130/80 mm Hg, a combination of two or more antihypertensive drugs is required. Thiazide diuretics can be used as first line monotherapy. Calcium channel blockers are also very effective especially in patients with IHD. ACE inhibitors and ARB are the drug of first choice for those patients who require renal protection. Atenolol is of usefulness in patients with effort angina or who have recent myocardial infarction. If monotherapy fails, combination therapy should be used.

National Kidney Foundation recommended blood pressure goal for patients with diabetes to be 130/80 mm Hg and 125/75 mm Hg for patients with albuminuria or frank proteinuria. ACE1 inhibitors are the first line drug for frank proteinuria. ACE1 inhibitors are the first line Drug.

Chapter 13

Gestational Diabetes Mellitus (GDM)

Gestational Diabetes Mellitus (GDM)

Dr. B.R. Giri MD.

Pregnancy is a stressful physiological condition. It results in important maternal changes in structure, metabolic and endocrine functions. The product of conception as a whole acts as a metabolic structure releasing various hormones, all these having diabetogenic impact to the mother. Pregnancy exerts a physiological challenge to insulin release and in the presence of diminished beta cell reserve, glucose intolerance result. Diabetes in itself is a complex metabolic disorder, resulting in several metabolic and physiological changes.

13.1. Diabetes in pregnancy

Diabetes in pregnancy can occur under different circumstances. These are as follows:

1. Pregnancy in Diabetes
 - Type 1 diabetes
 - Type 2 diabetes
 - Secondary diabetes
 - Impaired Glucose Tolerance before gestation
2. Gestational Diabetes
3. IGT of pregnancy
4. Undiagnosed pre-existing diabetes
5. Undiagnosed pre-existing IGT

Definition of Gestational Diabetes Mellitus :

Freinkel, in 1985 defined GDM as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy

13.2. Risk factors to GDM

Following are some important risk factors to developing GDM. These risk factors must be elucidated during initial consultation in the ANC clinic. In the presence of one or more risk factors, special care must be initiated and GDM looked for at appropriate time.

- Maternal age more than 25 years
- Multiparity
- Previous history of large or small baby
- Previous history of GDM
- Bad obstetric history viz. still birth, abortion, past pregnancy large baby
- Family history of diabetes

- Overweight pre-pregnant status
- Ethnic origin
- Patients own birth weight >4 kg
- Random blood sugar > 140 mg%
- Excess weight gain during pregnancy

13.3. Why is it important to treat GDM

Any amount of abnormal glucose intolerance result in deleterious effects in the foetus as well as in the expectant mother. This is also an indicator to increased risk of diabetes and cardiovascular diseases in mother as well as child later in life.

- Increased risk of maternal and fetal morbidity and mortality during pregnancy
- Mother is at increased risk of Type 2 diabetes in the future
- Baby is at risk of Type 2 diabetes, overweight and cardiovascular disease later in life

13.4. Manifestations of untreated GDM

Untreated GDM may result in manifestation of one or more of the following in the pregnant mother and unborn foetus.

13.4.1. Diabetes related

- Lethargy
- Thirst
- Urinary tract infection
- Pregnancy induced hypertension
- Recurrent thrush and UTI
- Increased rate of DKA
- Acceleration of chronic diabetes complications
 - Retinopathy
 - Nephropathy
 - Neuropathy
 - Cardiovascular events

13.4.2. Obstetric

- Polydramnios
- Premature labour
- Prolonged labour
- Vaginal tear and or episiotomy
- Instrumental delivery or Caesarean section
- Miscarriage

- Post partum haemorrhage
- Post partum infection

13.4.3. Risks of GDM to fetus

There is a wide range of perinatal problems related to diabetes. The risks occur from in utero to adulthood. Some of the common perinatal problems are as follows:

- Foetal death in utero
- Prematurity
- Small or large for gestational age
- Macrosomia
- Jaundice
- Hypoglycaemia
- Respiratory distress syndrome
- Hypertrophic organs
- Risk of diabetes and cardiovascular disease later in life

Risk of development of above complications is reduced on early and strict control of blood sugar during the gestational period. Congenital malformations are seen in GDM upto three times more than in general population.

13.5. Screening GDM

All pregnant women must be screened for presence of gestational diabetes mellitus. GDM is asymptomatic and hence the need of screening. If an expectant mother has one or more risk factors of GDM, she should be screened at the earliest opportunity. However, if no risk factors exist, she must be screened as per the protocol.

Following are the recommendations of 4th International Conference on GDM by American Diabetic Association in 1997:

13.5.1. When should the be screening be done

Screening must be initiated between 24th to 28th gestation weeks. However if one is not screened in this period, one may be screened later.

13.5.2. Who should under go the screening

All pregnant women must undergo screening

13.5.3. How is the screening done

- No preparation is required. This can be performed at any time of day regardless of meal.
- 50 grams oral glucose mixed in 250 ml water and drunk in 5 minutes
- Sit quietly for 1 hour
- Venous plasma glucose level is measured after 60 minutes
- Blood glucose level < 140 mg% indicates that GDM is not present
- Blood glucose level $\geq$ 140 mg% tests positive for GDM

13.5.4. Oral Glucose Tolerance in Gestational Diabetes Mellitus

Patients who test positive for GDM on initial screening and those who have strong risks for GDM must undergo oral glucose tolerance at 28 weeks of gestation or thereafter.

75 gram oral glucose tolerance test

- 3 days of unrestricted carbohydrate diet, no smoking, no alcohol for 24 hours
- Overnight fast 8 – 10 hours
- Venous plasma glucose level fasting tested
- 75 grams oral glucose mixed in 250 ml water and drunk in 5 minutes
- Remain seated throughout the test
- Venous plasma glucose level taken after 120 minutes

Fasting Blood Glucose Level >110 mg/dl is diagnostic of GDM

Formal 120 min Blood Glucose Level >140mg/dl is diagnostic of GDM

13.6. Clinical targets in Pregnancy

All pregnant women must maintain the measurable clinical parameters as near normal as possible.

Some of the more important clinical parameters that must be evaluated periodically are as follows:

Weight change should be positive in pregnancy

Overweight	7-10 kgs
Normal	10 - 12 kgs
Underweight	10 – 14 kgs

Blood glucose levels

Fasting	< 90mg/dl
1hr	<140mg/dl
2hr	$\leq$ 126mg/dl

Blood pressure

<130/70

Ketones in urine – negative

13.7. Care of expectant women with GDM

Care of women with GDM does not differ substantially from care required in diabetes in other situations. However, it is noticed that meticulous control of diabetes in pregnancy reduces risks of acute as well as chronic complications significantly both in mother and fetus.

Following are broad principles of care of diabetes in pregnancy:

- Eating Plan
- Exercise
- Medication
- Monitoring
- Regular obstetric and diabetes review

13.7.1. Diet in diabetes in pregnancy

A dietitian or a diabetic nurse provides medical nutrition therapy. Diabetic mothers need the same food they need in non-diabetic state. It is only the quantity and frequency of feeding that differs.

- Assess the patient's food consumption pattern and recommend individualized meal plan
- One must achieve optimal weight gain and hence balance calorie recommendation with weight gain
- Weight gain must be around 10 kg in the entire pregnancy
- Diet in first trimester must be as in non pregnant state
- Calorie intake must be 30 to 32 Kcal /kg for ideal weight in 2nd and 3rd trimester
- The individual must eat three meals and three snacks distributed at equal interval in the entire day.
- Distribution of calorie must be Carbohydrate 40-55% (150 to 200 gm per day), Protein 18-20% (1.2 to 2 gm/kg body weight), Fat upto 30%
- Advise to take high fiber and complex carbohydrate
- Regular intake of meals and snacks is important

13.7.2. Physical exercise in GDM

- Exercise increases insulin sensitivity, lowers blood glucose level, and

increases well being and fitness level.

- Choose light to moderate exercise that can be maintained throughout pregnancy
- Exercise 60 minutes a day, at least 5 days a week
- Exercise should include aerobic and resistance training eg, walking, swimming or water exercises, upper arm exercises etc.

13.7.3. Medication in GDM

Oral Hypoglycemic agents

Oral hypoglycemic agents are not recommended in pregnancy and hence stop OHA if a pregnant woman is taking. Switch over to insulin.

Insulin

Insulin is used to manage hyperglycemia in GDM when it is not controlled by diet and exercise. Short and intermediate acting insulin are preferred. Human mono-component insulin is better as formation and trans-placental influx of antibodies is avoided. Insulin requirement increases progressively with progression of pregnancy due to increasing insulin resistance. Insulin is given two to four times a day depending on the requirement.

13.7.4. Medical and obstetric follow up in GDM

Medical and obstetric review and monitoring of pregnancy is important. At each visit to the ANC, following parameters must be monitored.

- Blood pressure
- Blood glucose levels
- HbA1C at 3 month interval
- Weight change
- Other conditions i.e. urinary tract infection, vomiting
- Foetal growth, movement and lie of baby

13.8. GDM management during labor and delivery

Gestational diabetes mellitus need to be managed adequately during labour and delivery. The need for hospital admission depend upon metabolic control, fetal and obstetrical problems. However, for all practical purposes, it is safer to have an institutional delivery.

- Aim at delivering a normal sized, full term baby
- Continue pregnancy upto 38 weeks if every thing is all right
- In labour check blood sugar 1 to 2 hourly
- Hyperglycemia in later weeks of pregnancy will cause neonatal

hypoglycemia due to hyperinsulinism in foetus

- In case of elective Cesarean section, it should be done as the first case in the morning
- Unless blood sugar is >140 mg/dl, insulin glucose infusion is not required
- After placental delivery, insulin requirement falls abruptly by 25 to 50%
- Vaginal delivery is the safest and preferred mode of delivery

13.9. GDM management after delivery

Management of GDM continues following delivery and after discharge. GDM is a precursor of diabetes in post-pregnancy period.

Following delivery

- Monitor mother for blood glucose, infections and other complications of delivery
- Look for neonatal hypoglycemia, hypocalcaemia, respiratory distress
- Breast feed the child

Prior to discharge

- Lifestyle education must be given to the mother for both mother and baby.
- Nutrition assessment of both mother and child must be done and necessary diet advice given.
- Arrange for 75gram Oral Glucose Tolerance Test (OGTT) at 6 weeks postpartum period. This is necessary as 50 to 60% of GDM convert to overt diabetes mellitus and other 50% revert to IGT. Also advise yearly OGTT to reclassify them.
- Those patients with normal OGTT after delivery must be termed previous abnormality of glucose tolerance of statistical risk.
- Those GDM patients with postpartum abnormal OGTT must be termed either IGT or DM in non-pregnant adult

13.9.1. After a GDM pregnancy, establish goals for lifestyle behavior

A mother who has been established to have GDM must change lifestyle and be vigilant of blood sugar levels. She must follow the following:

- healthy eating
- planned regular exercise
- aim for ideal weight
- stop smoking
- method of contraception – plan each future pregnancy
- regular review of glucose tolerance status – OGTT each year and before

a planned pregnancy and when symptoms and signs are present

13.10. Importance of planning pregnancy in IGT or Diabetes

When an individual who knows of her IGT or diabetes status wishes to conceive, proper planning of pregnancy must be done.

Evaluation of HbA1c and glucose prior to and during pregnancy minimize the risk of:

- Congenital malformation
- Intrauterine death
- Maternal morbidity
- Fetal morbidity
- Complications during pregnancy, at delivery and post partum

13.10.1. Complications to fetus

Complications to fetus differ for different trimester of pregnancy. Following are some known complications to fetus at different trimester.

1st Trimester

- Congenital anomalies
- Miscarriage

2nd and 3rd Trimester

- Placental insufficiency
- Prematurity
- Respiratory distress syndrome
- Jaundice
- Macrosomia
- Hypertrophic Cardiomyopathy
- Death in utero
- Neonatal Hypoglycaemia
- Foetal distress in labour
- Shoulder dystocia
- Birth Injuries

13.10.2. Maternal complications

The pregnant mother too can sustain various short term as well long term effect due to pregnancy in diabetes. Mothers may develop obstetrical complications during pregnancy or during labour.

Following are some maternal complications due to pregnancy in diabetes.

Diabetes Related

- Thrush and UTI
- Pregnancy induced hypertension
- Higher rate of DKA and hypoglycaemia
- Hypoglycaemic unawareness
- Acceleration of chronic diabetes complications
 - ♦ Retinopathy
 - ♦ Nephropathy
 - ♦ Neuropathy
 - ♦ Cardiovascular events

Obstetric Complications

- Polyhydramnios
- Miscarriage
- Premature labour
- Pregnancy induced hypertension
- Prolonged labour
- Instrumental delivery
- Caesarean section
- Post partum haemorrhage
- Post partum infection

13.11. Preconception care

When pregnancy is planned, following are some preconception measures that a woman contemplating pregnancy must do. However, it must be noted that even otherwise, meticulous control of blood sugar is recommended even for non-pregnant state to slow progression of diabetic chronic complications.

- Contraception should be used until glycaemic control is satisfactory. Near normalisation of blood sugar is targeted preconception as well as during the first 6-8 weeks of pregnancy
- When pregnancy planning is desired, oral antidiabetic agents must be changed to Insulin atleast three months before trial of conception when HbA1c level is achieved to < 6.5%
- Periodic complications assessment must be carried out viz. renal function, cardiovascular status and retinal evaluation
- Glycaemic control of HbA1c of < 6.5% must be maintained
- Diabetes self care skills and knowledge must be taught and assessed.
- Nutrition assessment and adequate nutrition planning must be done.

13.12. Future care

Diabetes in pregnancy must be on regular follow up as any other diabetic after the pregnancy is over. These patients must follow all measures as any other diabetic.

- Regular clinic visit to monitor glycaemic control
- Periodic complication assessment
- Aim HbA1C < 6.5%
- Contraception
- Plan each future pregnancy

Regular review of glucose tolerance status for those with IGT must be done. Oral glucose tolerance test must be performed each year and when symptoms or signs are present

Chapter 14

Diabetes in children

Diabetes in children

Maj (Dr.) H.P.Chhetri. MD

As in the adults, the major forms of diabetes are divided into two main groups. Type 1 Diabetes is the most common endocrine-metabolic disorder of childhood and adolescence. Type 2 Diabetes is usually seen in obese children at adolescence, also sometimes called as MODY (Maturity onset Diabetes of Young).

14.1.Type 1 Diabetes

Formerly called IDDM or juvenile onset Diabetes mellitus, Type1 diabetes is characterized by low or absent levels of endogenously produced insulin. The onset is usually in childhood with median age of 7 to 15 years, but can present at any age. It is due to autoimmune destruction of pancreatic Islet beta cells. Usually presentation in children may be with acute complications, primarily ketoacidosis or with features of malnutrition. Duration of symptoms is short, lasting usually 2-3 weeks or less. Classical symptoms of Type 1 diabetes are polydypsia, polyuria, polyphagia, decreased activity and significant weight loss. In children nocturnal enuresis may often be noticed. Prolonged hyperglycemia and lack of insulin lead to progressive calorie depletion which presents with increased appetite and weight loss.

14.2. Type 2 Diabetes

Though Type 2 Diabetes is seen beyond 40 years of age, it has been increasingly observed in children and adolescents as well.

Like in the adults, sedentary lifestyle and obesity are the main contributing factors to the disease. These children have a strong family history of diabetes and the disease presents at around 15 to 16 years of age. There is a strong association with insulin resistance.

As definitions, epidemiology, etiology, pathogenesis and diagnosis are dealt in other chapters, only the management part, particularly directed towards the pediatric age group will be considered in this chapter.

14.3. Management of diabetes in children

Diabetes is a complex issue, management requires a team approach consisting of pediatrician, diabetic nurse/educator, dietician and a social worker.

14.3.1.Principles of therapy

Following are some guiding principles in the management of diabetes in chil-

dren. These principles must be followed to ensure optimal growth and development in a child living with diabetes.

- 1 Elimination of clinical features of uncontrolled diabetes
- 2 Prevention of DKA
- 3 Avoidance of hypoglycemia
- 4 Maintenance of normal growth and development
- 5 Early detection of associated diseases
- 6 Prevention of emotional disorders
- 7 Prevention of chronic vascular complications

14.3.2. Goals of therapy

1. Maintain balance between glucose control and hypoglycemia.
2. Eliminate polyuria and nocturia.
3. Prevent ketoacidosis.
4. Permit normal growth and development with minimal effects on lifestyle.

14.3.3. Specific therapeutic objectives of management

Following are some very specific therapeutic objectives in managing a child with diabetes. These objectives must be met as near as possible for optimal management of a child with diabetes.

- 1 Glycosylated hemoglobin: 3 monthly - 6.5% or lower
- 2 Self monitoring of blood sugar daily before meal and at bedtime (fasting 80-110 mg/dl and other 80-140 mg/dl)
- 3 Urine testing of sugar and ketones (first voided sample in the morning)
- 4 Urine testing for proteins (of single voided urine at each visit)
- 5 Serum lipids (cholesterol, HDL, LDL, VLDL fractions and triglycerides annually should be normal)
- 6 Thyroid function tests once annually should be normal
- 7 Eye evaluation including fundus examination annually by an ophthalmologist. More frequent examinations advised if vascular changes are noted.
- 8 Examination of teeth and gums by a dental hygienist/dentist once every 6 month

14.3.4. Some aspects of diabetes management in children

The main aspects of overall management of diabetes in childhood can be broadly divided into the following.

1. Insulin therapy
2. Nutrition
3. Exercise and physical activities
4. Psychosocial aspects
5. Diabetes education

14.3.4.1. Insulin therapy

Type 1 diabetes is managed with insulin. Various types of insulin preparations and their duration of actions have been already covered (ref chapter 7)

The requirements of insulin in children differ at different age groups. The following table shows subcutaneous insulin dosing.

Table 14.1 : Subcutaneous insulin dosing

Age in years	Target glucose (mg/dl)	Total daily Insulin (unit/kg/dose)	Bolus insulin Units to be Added per 100mg/dl above target
0-5	100-200	0.6-0.7	0.5
5-12	80-150	0.7-1.0	0.75
12-18	80-150	1.0-1.2	1.0-2.0

Most of the children are placed on combination of intermediate (*lente*) and short acting (*regular*) insulins 20 to 30 minutes before breakfast and dinner using highly purified porcine or human insulins. The initial requirement may range from 1-1.75 units/kg/day. Subsequently a partial remission may occur and requirement of insulin may decrease to 0.5-0.6units/kg/day (“honeymoon”). Eventually insulin requirement increases to a plateau. The *split-mix regime* is generally practiced. In this practice the 2/3rd of the total dose is given before breakfast and 1/3rd before dinner. The 2/3rd of each dose of insulin will be *lente* and 1/3rd *regular* insulin. The adjustment of dose of insulin requires monitoring of blood sugar, urine sugar, ketone bodies in the urine, diet and exercise. Premixed Insulin (Mixtard 30:70) is available along with short and intermediate acting Insulin in the Essential Drug List.

It is important that parents and children with diabetes are educated about the types of insulins and purity of various types of insulin. The technique of injection, use of disposable syringes, and selection of sites and rotation of sites for injection should be discussed extensively. Elder children should be encouraged to inject themselves. The injection sites should be inspected in each visit as far as possible. Above table roughly guides requirement of insulin. However, dose of insulin is dependent on several factors and may vary from a child to another.

14.3.4.2. Nutrition

Nutrition plays an important role in the management of children with diabetes mellitus. This is of critical importance during childhood and adolescence as appropriate energy intake is needed to meet the energy expenditure for growth and pubertal developmental requirements. On the other hand nutritional treatment along with insulin or other measures in combination relieves symptoms of hyperglycemia and prevents long term complications of diabetes mellitus. The recommended caloric intake based on size and surface of the child can be obtained from standard table. The calorie intake should comprise approximately 55% of carbohydrate, 30% fat and 15% protein. The table below shows the calorie requirement of children and young adults.

Table 14.2 : The calorie requirement of children and young adults

Age	Kcal required/kg body weight (mean)
Children	
0-12 months	120
1-10 years	100-75
Young women	
11-15 years	35
Young men 11-15 years	65

There is a gradual decline in calorie requirement as age increases.

The table below shows a summary of nutritional guidelines for children/ adolescence with Type 1 diabetes mellitus.

Table 14.3 : Nutritional Guidelines for children and adolescents in Type 1 Diabetes

Nutrition	(%) of calories	Recommended daily intake
Carbohydrate	Will vary	
Fiber	>20 g per day	High fiber , especially soluble
Protein	12-20	
Fat	<30	
Saturated	<10	
Polyunsaturated	6-8	
Monounsaturated	remainder of fat allowance	

The achievement of nutritional goal requires cooperation of the diabetic child as well the parents. The child can take all food that h/she was initially taking. The division of meal is done into three major and three mid-meal snacks to avoid hypoglycemia. A healthy diet is the same for everyone, whether or not they have diabetes. The whole family should be eating the same food. Sweets are no longer off limits because the 'diabetic diet' is now a relic of the past. Once the child gets to know how the body responds to eating and taking insulin, sweets in moderation are possible accompanied by the appropriate dose of insulin. However it is important to get long term glycemic control by the child for optimal growth and prevention of complications of diabetes. The total calorie intake can be divided so that breakfast provides 20%, lunch 20% and dinner 30%, and rest of the 30% is left for in-between meals for mid-morning, mid-afternoon and evening. This is done to ensure a stable blood glucose level, avoiding a big surge of blood sugar following intake of large quantity of food and episodes of hypoglycemia in between meals. Emphasis should be placed on regularity of food intake and consistency of carbohydrate intake. Adjustments in meals planning must be made depending upon the need and desire of individual child. Nutrition must be adequate to ensure that the child continues to grow physically.

14.3.4.3. Exercise and physical activity

Exercise, including competitive sports, should not be forbidden to the diabetic child. Exercise increases glucose utilization. Insulin requirement of highly fit child is less and they have better metabolic control. It also improves self image. Exercise should include walking, jogging, swimming and games like tennis etc. Each patient with guidance of physician and under parental supervision should develop an appropriate regime for regular planned exercise. Adjustment of insulin dose and diet should be taught according to the requirement. Early signs of hypoglycemia should be recognized and appropriate measures taken in terms of correction and adjustment of insulin dose.

14.3.4.4. Psychosocial aspects

The health worker must understand the effect of diabetes on the child as well as the family. Diagnosis and long term management offers a challenge to the child and the family requiring acquisition of knowledge and skill for insulin administration, blood testing, urine testing, interpretation of signs etc. The family should assume the prime treatment responsibility with the health worker and other members of team acting as consultants.

14.3.4.5. Diabetic education

The children and the parents of the diabetic children need ongoing educational and emotional support from health workers. The educators should be able to

make them aware of the need of achieving near normal blood sugar and level of HbA1c in preventing chronic complications of diabetes. The risk of developing hypoglycemia as an adverse effect of intensive therapy should also be explained. Meticulous management will need achievement of expertise in insulin administration and blood sugar monitoring at home.

14.3.5. Management of Diabetic ketoacidosis in children

Clinical signs, symptoms, and diagnosis of diabetes ketoacidosis have been already covered in the chapter on complications of diabetes (chapter 8). Management aspect pertaining particularly to children is dealt here in this section. More than 20% of children with diabetes present with features of diabetic ketoacidosis at the time of initial presentation.

Goals of treatment of DKA

1. Intravascular volume expansion
2. Correction of deficits in fluids, electrolytes, and acid-base status
3. Initiation of insulin therapy to correct catabolism, acidosis

14.3.5.1 Fluid therapy

Replacement of fluid is essential for hemodynamic stability as well as correction of acidosis. The initial fluid should be Normal Saline given in a dose of 20 ml/kg within first hour. Saline should be given slowly thereafter till signs of severe dehydration are corrected. Blood sugar level should be monitored hourly and when sugar level falls below 300 mg/dl, 5% Dextrose should be added to the infusion.

14.3.5.2 Treatment of electrolyte abnormalities

Serum potassium is often elevated, though total body K⁺ is depleted. Potassium is started early as resolution of acidosis following administration of insulin will cause a decrease in serum K⁺. It is given in a dose of 1ml/L of IV fluid given. Never give potassium if the child has not passed urine. Bicarbonate is almost never administered except in *severe* acidosis leading to cardio respiratory compromise.

14.3.5.3 Insulin Therapy

Continuous low dose intravenous infusion of insulin is the most preferred way of managing DKA in children. An initial bolus of 0.1 unit/kg followed by a continuous IV infusion at a rate of 0.1 unit/kg/hr. The main aim is to reduce blood sugar at the rate of 50-100 mg/dl per hour. The usual practice is to add 1 unit/kg of plain insulin in 100 ml of 0.9% saline and infuse at the rate of 10 ml/hour. The dose can be reduced to 0.05 units/kg/hr once blood sugar level falls

below 200 mg/dl. The infusion can be discontinued once blood sugar has levelled to normal range. Give subcutaneous insulin at least 30 minutes before discontinuing the infusion.

14.3.5.4 Monitoring

Monitoring the patient is an important aspect of DKA management. Close monitoring of vital sign, blood sugar, state of consciousness and urinary ketone is necessary till intravenous infusion is required. Urine out put should be checked every 4 hour. Electrolytes and blood gas analysis should be done every 2-4 hour depending on the degree of acidosis till the first 12 hours of initiation of therapy where ever such facilities are available.

Chapter 15

Diabetes and Mouth care

Diabetes and Mouth care

Dr. Karma Tobgyal MD

Diabetes Mellitus is a chronic metabolic disorder characterized by a relative or absolute lack of insulin that results in elevated blood glucose levels and it produces disturbances in lipid and protein metabolism.

With increasing disease prevalence, it has become critical for the dental practitioner and other health professionals to.

1. Recognize signs and symptoms of diabetes, to facilitate early diagnosis and management.
2. Manage oral conditions, to maxima.

15.1. Diabetes and mouth

Infection, inflammation and poor wound healing in the mouth are some manifestations of diabetes. Besides hypoglycemia, ketoacidosis and vascular wall disease increases susceptibility to infection.

There is increased incidence of persistent gingivitis, periodontal abscess and chronic periodontal diseases. Because micro vascular disease in periodontium adversely affects blood flow and leukocyte migration, predisposing to premature periodontal disease, abscess and delayed wound healing, oral candida also occurs more frequently in diabetics due to altered response to infection and xerostomia.

Burning tongue can be due to fungal infections such as candidiasis, or peripheral neuropathies, Associated with diabetes, xerostomia may be due to hyperglycemia and subsequent polyuria that depletes extracellular fluids, which leads to reduction in secretion of saliva.

Good glycemic control and meticulous home care are cornerstones in the prevention and care of oral ulcers, infections, dental caries, and alveolar bone loss because of periodontitis associated with diabetes

15.2. Periodontal disease

Periodontal disease is a chronic bacterial infection that affects gum and bone supporting teeth. It is a serious infection that, if left untreated, can result in tooth loss. In untreated cases, periodontal disease can be life threatening for diabetic patients. The disease can affect one or many teeth. It begins when the bacteria in plaque-the sticky, colorless film that constantly forms on teeth- cause the gums to become inflamed.

Gingivitis is often caused by inadequate oral hygiene and is reversible with professional treatment and good oral home care. Untreated gingivitis can advance to periodontitis. Gums separate from teeth, forming pockets-spaces be-

tween teeth and gum- that become infected. As disease progresses, the pockets deepen and more gum tissue and bone are destroyed. Teeth can become loose, the way the teeth bite together may change and teeth may be lost.

15.3. Factors influencing the health of gums

Several factors influence the function of teeth and gums. Some are man made and the others natural.

- Genetics
- Pregnancy and Puberty
- Smoking and tobacco use.
- Stress
- Medications.
- Clenching and grinding teeth
- Diabetes.

People with diabetes are more likely to have periodontal disease than are people without diabetes, probably because diabetics are more susceptible to contracting infections.

Those people who don't have their diabetes under good control are especially at risk of dental and periodontal problems. A recent study demonstrated that poorly controlled Type 2 diabetic patients are more likely to develop periodontal disease than those who have good control of diabetes.

- More than half of all adults have, at least, early stages of gum disease.
- About 90 percent of adults have gum disease at some time during their lives.
- People with diabetes are at higher risk for gum problems and tend to have more gum disease and infections.
- Patients can be educated about gum disease and its prevention, and it is here that the medical professional plays an important role by encouraging meticulous daily oral hygiene practice.
- Patients should be alerted of early signs of gum disease, such as bleeding or slight gum discomfort.
- **Six monthly dental visits are important;** more often if there are problem.
- For edentulous (without teeth) patient, yearly visits are recommended for checking the health of the tissues and to detect possible infection.

15.4. Oral Hygiene in Diabetes

Long term studies have proven the value of consistent and regular oral hygiene care routines. Regular and timely dental visits are imperative to reinforce those habits and to minimize oral health problems. The basics of oral care for all people include brushing, flossing, mouth rinsing and tongue cleaning. Special care in many of those areas is of utmost necessity for people with diabetes.

15.4.1 Tooth brushing

Teeth should be brushed at least twice daily with soft brush. If possible, teeth also should be brushed after meals. The use of a brush with soft bristles is very important. Stiff bristle or too rigorous brushing can damage the gums and increase potential problems.

15.4.2 Flossing

Patients also should be encouraged to floss. Ideally teeth should be flossed at least once daily. Again, a wide array of flossing products are available. Several types of flossing tools designed to make flossing easier are also available.

15.4.3 Mouth rinsing without alcohol content

Mouth rinsing also can be a part of good oral health, but should be taken to select a mouth rinse that meets the patient's specific needs. Some mouth rinses have fluoride and are intended to decrease cavities. Those mouth rinses typically have little effects with regard to gum disease and bad breath. Other products are intended to be used before brushing and are for the purpose of increasing the effectiveness of brushing. For people with diabetes the greatest areas of concern tend to be with gum disease and bad breath. Those people need a mouth rinse that addresses bacteria and by-products of bacteria that contribute to gum problem.

- The relationship between diabetes and periodontal disease goes both ways, each making the other more difficult to manage.
- People with diabetes are at higher risk of gum disease.
- Diabetes should use a toothbrush with soft bristles.
- Alcohol in mouth rinses can dry mouth and result in exacerbation of oral health problems.
- The tongue also can harbor bacteria and regular tongue cleaning is recommended.

15.5 Conclusion

People with diabetes are more likely to have periodontal disease than are people without diabetes. Furthermore, studies have found a link between periodontal disease and coronary artery disease in Type 1 diabetic adults.

Those people who don't have their diabetes under control are especially at risk. Poorly controlled Type 2 diabetes patients are more likely to develop periodontal disease than are well-controlled diabetes.

Chapter 16

Hospitalization in Diabetes

Hospitalization in Diabetes

Dr. B.R. Giri MD.

Most diabetics can be managed on outpatient basis. These patients have to be followed up regularly and patient and family members must participate actively in the management. However, it must be remembered that these patients may need hospitalization and meticulous indoor management occasionally. There are certain indications for hospitalization. The physician must “err to the higher side” for hospitalizations and at the earliest need, these patients must be hospitalised.

16.1 Indications for hospitalization

Following are some indications for admitting diabetic patients in hospital and manage intensively.

Delaying admission can be deleterious for the health of the patient. Hence, these patients must be hospitalized at the earliest indication for admission.

16.1.1. General indications

- Life threatening acute metabolic complications of diabetes.
- Newly diagnosed diabetes in children and adolescents.
- Substantial and chronic poor metabolic control that necessitates close monitoring of patient to determine etiology of the problem with subsequent modification of therapy.
- Severe chronic complications of diabetes that require intensive treatment or other severe condition unrelated to diabetes that significantly affect control or are complicated by diabetes.
- Uncontrolled or newly diagnosed insulin requiring diabetes during pregnancy, GDM requiring insulin.
- Major modification of fixed insulin treatment regimens or to initiate insulin treatment in those who were on OHA.

16.1.2. Acute Metabolic Complications of Diabetes

16.1.2.1 Diabetic Ketoacidosis

- Blood glucose >250 mg/dl.
- Arterial pH <7.35, Venous pH <7.30, or Serum bicarbonate level <15 mEq/l and
- Ketonuria and/or ketonemia.

16.1.2.2. Hypoglycemia with neuroglycopenia

- Blood glucose <50 mg/dl and the treatment of hypoglycemia has not resulted in prompt recovery of sensorium
- Coma, seizures, or altered behavior (e.g. disorientation, unstable motor coordination, dysphasia) due to documented or suspected hypoglycemia
- Hypoglycemia has been treated, but a responsible person can not be with the patient for ensuing 12 hours
- Hypoglycemia was caused by a sulphonylurea or insulin.

16.1.2.3. Hypersomolar nonketotic coma

Impaired mental status and elevated plasma osmolality in a patient with hyperglycemia. This usually includes severe hyperglycemia (e.g. >400 mg/dl) and elevated plasma osmolality >315 mmol/kg). Ketonuria and ketosis is not demonstrated.

16.1.2.3. Uncontrolled Diabetes

Poor metabolic control of established diabetes as defined herein justifies admission if it is necessary to determine the reason of poor control and to initiate corrective measures.

- Hyperglycemia associated with volume depletion
- Persistent refractory hyperglycemia associated with metabolic deterioration.
- Recurring fasting hyperglycemia >300 mg/dl that is refractory to outpatient therapy
- Recurring episodes of severe hypoglycemia (i.e. <50 mg/dl despite intervention.
- Metabolic instability manifested by frequent swing between hypoglycemia (<50 mg/dl and fasting hyperglycemia (>300 mg/dl)
- Recurring diabetic ketoacidosis without precipitating infection or trauma.

16.1.2.4. Chronic complications of Diabetes

Certain chronic complications of diabetes like foot ulcer, chronic renal failure, severe retinopathy or ischaemic heart disease etc need hospitalization to initiate corrective or preventive measures.

Chapter 17

Preventing Diabetes, the way Forward

Preventing Diabetes, the way Forward

Dr. B.R. Giri MD.

Diabetes mellitus is a chronic metabolic disorder. It is associated with a wide range of complications. However, complication occur due to exposure of an individual to high blood sugar over a prolonged period of time.

There are substantial evidences now that Type 2 diabetes can be prevented from occurring as well as that complications of diabetes are either prevented or are delayed from occurring. Progression of complications too can either be slowed or halted.

17.1 Primary prevention

Primary prevention refers to preventing diabetes from occurring. It is known beyond doubt that certain conditions predispose an individual to contracting diabetes. Diabetes can be prevented or delayed from occurring if these conditions are made known to individuals and that they avoid those known risk factors.

17.1.1. Preventing Type 2

There are certain modifiable risk factors that predispose one to developing Type 2 diabetes. These risk factors are as follows:

- Obesity
- Physical inactivity
- High blood pressure

Other risk factors that can not be modified are age above 40 years; a parent, sister or brother has diabetes, had diabetes in pregnancy and any women who gave birth to a large baby (> 4 kg).

Research has shown that Type 2 diabetes can be prevented from occurring by modifying life style and changing some eating habits. This is especially so in people more than 60 years of age.

17.1.1.1. Making wise food choices

You may not have developed diabetes but are at risk of getting it. What you eat has a big impact on your health. Make wise food choices to keep your body weight under control, normal blood pressure and normal cholesterol levels.

You can eat all types of food that you were eating earlier but follow the following basic rules:

- Reduce serving size of the main meals that you eat especially of those that contain high fat like dessert, meat, cake.
- Increase amount of intake of vegetables containing high fiber. Half of your meal must contain vegetables

- Eat fruits in moderation
- Limit your fat intake to less than 20% of total calorie intake of the day. Some practical tips of reducing fat intake are:
 - do not eat fried food
 - avoid eating fat containing meat,
 - remove skin of chicken before cooking,
 - avoid eating nuts
 - avoid fast food, fried potato wafers etc
- Reduce your total calorie intake if you are overweight. Your diabetic nurse or dietician will help you plan your meals
- You can eat low calorie food in any amount like green salad without topping, 'chinta', tea without sugar, 'dau' and spices to your taste.
- Keep a record of what you eat for the entire day. You will know for yourself where you are.

17.1.1.2. Increasing physical activity

Physical inactivity is one of the most important reasons of overweight and obesity. Physical inactivity also results in insulin normally produced in body to be insensitive and its action being less efficacious. All these contribute to developing Type 2 diabetes

Increasing physical activity improves insulin sensitivity and prevents diabetes from manifesting.

It is important first of all to initiate physical activity. The activity must be gradually increased, adding a few minutes each day. One must exercise at least 60 minutes each day for all days of a week.

Physical activity can be brisk walking, jogging, playing, gardening, going around chorten etc.

Physical activity must be continued for life time.

17.1.1.3. Maintaining a reasonable body weight

Body weight affects health in many ways. Obesity is a contributing factor of several disease conditions.

Body Mass index is a measure of body weight relative to height. BMI can be used to see whether one is underweight, normal weight, overweight or obese. BMI is calculated by dividing weight in kilograms by height in meters squared.

$$\text{BMI} = \text{kg/m}^2$$

BMI can also be measured by using BMI chart.

Find height in centimeters in the bottom of the chart.

Find weight in kilograms in the right hand side of the chart.

Move along the row and column of weight and height to find the intersecting point.

The number at the intersection is the BMI. Check whether your BMI is normal or abnormal.

Risk of associated disease according to BMI & Waist circumference

Body Mass Index	Grade	Waist < 40 inches in men & <35 inches in women	Waist > 40 inches in men & > 35 inches in women
18.5 or less	Underweight		
18.5 to 24.9	Normal		
25 to 29.9	Overweight	Increased	High
30 to 34.9	Obese	High	Very High
35 to 39.9	Highly obese	Very High	Very High
40 or greater	Extremely obese	Extremely High	Extremely High

If one is overweight or obese, choose sensible ways to get in shape.

- Decrease amount of food that you generally eat.
- Limit amount of fat intake
- Increase your physical activity. Exercise most days of week. Aim at least 60 minutes of exercise each day.
- Set a reasonable goal of losing at least 500 grams a week and a long term goal of maintaining your BMI at 24 to 25.
- Avoid crash diet

17.1.1.4. Other modifiable factors for diabetes prevention

Following are some other modifiable risk factors to diabetes. These must be looked for periodically and adapt life style measures to prevent contracting them. This is more so after 40 years of age.

Hypertension

Check blood pressure at every opportunity. Persons with high blood pressure develop diabetes. If one already has hypertension, keep it under good control by adapting life style change and medications.

Cholesterol

Check cholesterol and triglyceride at least once a year after 40 years of age.

These add to the risks of complications of diabetes.

Diabetes in pregnancy

If one had diabetes in pregnancy or gave birth to a baby more than 4 kg weight, one has high risk of developing diabetes. Check blood sugar at least once a year. Follow other life style modification measures.

Alcohol

Moderate or stop alcohol intake. If one is a non user, do not start drinking alcohol in any form.

Diabetes in family

If one has any one in the family (mother, father, brother or sister) who has diabetes, one is at increased risk of getting the disease. Be extra cautious, maintain normal body weight, remain physically active, keep a check of eating habit and undergo periodic medical check up.

- avoid eating fat containing meat,
- remove skin of chicken before cooking,
- avoid eating nuts
- avoid fast food, fried potato wafers etc
- Reduce total calorie intake if one is overweight. The diabetic nurse or dietician will help plan meals
- Eat low calorie food in any amount like green salad without topping, 'chinta', tea without sugar, 'dau' and spices to taste.
- Keep a record of what is eaten for the entire day. This is a way knowing ones eating.

17.1.2. Preventing Type 1 diabetes

There are limited measures of preventing Type 1 diabetes because definite preventive agents for causation of the disorder are not always identified. It is important to immunize all children with primary series of vaccines in their first year of age. Encourage exclusive breast feeding for the first six months of life.

17.1.3. Approaches to primary prevention

Primary prevention can be achieved by the following approaches

17.1.3.1. Population approach

Awareness on diabetes and its risk factors can be made through approaches like informing population through mass media, group education, school health, school curriculum etc.

17.1.3.2. High risk approach

Populations at risk are identified and stratified at increased risk of progression based on age, BMI, family history. These individuals must be aware of diabetes and benefits of weight loss and physical activity. It must also be understood that risk factors of Type 2 diabetes are also the risk factors of other non-communicable diseases.

17.2. Secondary prevention

Identifying diabetes and preventing microvascular as well as macrovascular changes in diabetes is secondary prevention. Studies have shown that upto 50% of diabetics at detection already have microvascular changes. Early detection of diabetes and initiation of treatment prevent micro as well as macrovascular changes from occurring and halt its progression if these have already occurred. It is important to ensure targets of glycaemic control.

17.3. Tertiary prevention

Institution of aggressive therapy in persons who already have diabetes to minimize consequences of diabetes is tertiary prevention. This ensures containment or delay of progression of complications that ultimately reduces morbidity, disability and mortality due to diabetes.

Table 17.2 : Strategies for Tertiary prevention

Lower limb amputation	Daily self foot examination Foot examination at every clinic visit Appropriate foot wear
Renal Failure	Meticulous blood pressure control Control of hyperglycemia Use of ACE inhibitors and ARBs Low protein diet if indicated
Cardiovascular disease	Control of hypertension Control of dislipidemia Stop smoking

Diabetes is increasing in epidemic proportions world wide. This is more so for the developing countries. It is estimated that most of the urban centers in the South East Regional countries have more than 10% of people with diabetes. The proportions may not have reached such heights in Bhutan but however, diabetes is certainly on a rise. The good news is that secondary and tertiary

prevention are highly effective. However, the approach must be primary prevention. More efforts must be invested now to increase awareness of the disease, its long term complications, risk factors and lifestyle changes required thereof in the would be diabetics who ultimately adopt life-style that are averse to the development of the disease. The path is arduous but it is real.

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