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PROMPT

Pakistan's Recommendations for Optimal Management of diabetes from Primary to Tertiary car level

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Published by: **National Association of Diabetes Educators of Pakistan**

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This edition is the revised edition of the

National Clinical Practice Guidelines 1999

These guidelines are solely designed to cover management of type 2 diabetes. Guidelines for special situations like type 1 diabetes, gestational diabetes, diabetes and Ramadan etc., to follow.

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PROMPT

Pakistan's Recommendations for Optimal Management of diabetes from Primary to Tertiary care level

EDITORS

Prof. A. Samad Shera

Prof. Abdul Basit

PROMPT CORE TEAM

Dr. Zahid Miyan

Dr. Musarrat Riaz

Dr. Asima Khan

Dr. Riasat A. Khan

Dr. Asher Fawwad

CO CONTRIBUTORS

Prof. Rubina Hakeem

Dr. Asim Bin Zafar

ADVISORY BOARD FOR THE CARE OF DIABETES (ABCD)

Prof. Waheed Iqbal

Prof. Jehangir Khan

Prof. Irshad Khoso

Prof. Qazi Masroor

Dr. Sobia Sabir

Prof. Zaman Shaikh

Dr. Salma Tanveer

Prof. Bilal Bin Younus

Prof. Jamal Zafar

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PREFACE

Pakistan is a developing country with limited resources and diverse socio-economic standards.

Pakistan has high prevalence of diabetes and its complications, which is a great challenge to the existing health care system. The major contributing risk factors are urbanization, lifestyle, maternal and foetal malnutrition and genetic factors.

National action plans for control of diabetes have been developed and initiatives have been taken but not at an ideal pace. Training of primary care physicians and development of multidisciplinary diabetes care teams was initiated. Prioritization strategies were defined according to the International Diabetes Federation (IDF) guidelines, highlighting diabetic foot, diabetes education and children with diabetes. Research for better understanding and management of diabetes in Pakistan was undertaken. Collaboration between various stakeholders was promoted at national and international level. In short, public private relationships and development of multifaceted approaches is expected to improve the lives of millions of people with diabetes in Pakistan.

First National Practice Guidelines for Pakistan were published in 1999. They were very helpful in standardizing the management of type 2 diabetes. In view of important developments in the field of diabetes during the recent years, it was felt that 1999 National Clinical Practice Guidelines edited by Prof. A. Samad Shera should be revised. Also with rapidly increasing number of diabetic patients and the escalating burden on health economy, it is essential to develop a primary to secondary / tertiary care referral system.

These guidelines are developed after an extensive research and cover many aspects of diabetes management; however it is not our intention to present them as a text book of diabetes.

We hope that these guidelines will help in improving the diabetes care in Pakistan.

A special word of thanks to the Members of the Advisory Board for the Care of Diabetes (ABCD), for their contribution.

Prof. Abdul Basit

Prof. A. Samad Shera

Foreword

As a part of its ongoing efforts to ensuring provision of high quality clinical services at all levels of the health care delivery system in Pakistan, the Ministry of National Health Services, Regulations and Coordination is committed to provide quality technical assistance and support for standardization and quality of care for Diabetes.

National Clinical Practice Guidelines are indicative of best professional standards of practice and excellent research work. We hope that the nationwide adaptation of these practices will standardize the management of diabetes at one hand and lead to the best outcome on the other. We expect a remarkable reduction in the burden of the disease as a result.

It is unreservedly stated that we support and endorse "National Clinical Practice Guidelines for management of Type 2 Diabetes (Revised edition 2016)", written by Prof. A. Samad Shera and Prof. Abdul Basit.

Due to increasing prevalence of Diabetes in Pakistan and enormous burden on healthcare, it is hoped that the use of these guidelines will contribute in improving the clinical practices and disease management, hence reducing the morbidity and mortality in Pakistan.

Muhammad Ayub Shaikh,
Secretary,
Ministry of National Health Services,
Regulations and Coordination,
Islamabad.

CONTENTS

CHAPTER 01

INTRODUCTION

Pakistan is the sixth most populous country of the world with estimated population of 189 million. Over 60 % of total population lives in rural areas. Poverty is one of our major issues, with majority having per capita income of only 4$. Health expenditure is only 2.6 % of GDP.[1] Pakistan faces health challenges in diabetes due to its high prevalence and its related complications.[2] The major contributing risk factors are genetic factors, maternal and foetal malnutrition with rapidly urbanizing lifestyle.

PROMPT guidelines are based on available local and regional scientific evidence (Evidence) including special considerations to affordability and availability of medicines and consensus statements by Advisory Board for Care of Diabetes (Recommendation).Table-I.

Table-I: How do strength and quality of evidence correlates.[3]

Category	*Quality Definitions*	*Strong Recommendation*	*Weak Recommendation*
High Quality Evidence	Further research is very unlikely to change our confidence in the estimate of effect	The working group is confident that the desirable effects of adhering to this recommendation outweigh the undesirable effects. This is a strong recommendation for or against. This applies to most patients.	The working group recognizes that the evidence, though of high quality, shows a balance between estimates of harms and benefits. The best action will depend on local circumstances, patient values or preferences.
Moderate Quality Evidence	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	The working group is confident that the benefits outweigh the risks, but recognizes that the evidene has limitations. Further evidence may impact this recommendation. This is a recommendation that likely applies to most patients.	The working group recognizes that there is a balance between harms and benefit, or that there is uncertainty about the estimates of the benefits and harms of the proposed intervention that may be affected by new evidence. Alternative approaches will likely be better for some patients under some circumstances.
Low Quality Evidence	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate or any estimate of effect is very uncertain.	The working group feels that the evidence consistently indicates the benefit of this action outweighs the harms. This recommendation might chage when higher quality evidence becomes available.	The working group recognizes that there is significant uncertainty about the best estimates of benefits and harms. Very weak recommendation, other alternatives may be equally reasonable.

These guidelines not only concentrate on diagnosis and management of diabetes but also provide a key to maintain referral system from primary to secondary and tertiary care and vice versa. Special emphasis has been given to develop the concept of multi disciplinary team for the management of diabetes and hence chapters on nutrition, physical exercise and diabetes education have been included. These recommendations will be revised every two years. Any major changes in the intervening period will be included as addendum/corrigendum.

These are only guidelines and hence individualized approach according to specific scenario is still the key to the management. These guidelines are only for type2 diabetes. Guidelines for type1 diabetes, gestational diabetes mellitus, Ramadan and diabetes and on diabetic foot will follow soon.

1. Type1 diabetes guidelines will be developed after the initiation of type1 registry by summer 2017. (Diabetes Registry of Pakistan DROP). The first step already taken is DROP 1 and registry is commenced in around fifty centers all over Pakistan.
2. Ramadan and diabetes guidelines have been developed by the IDF DAR alliance (Diabetes and Ramadan alliance).[4] Regional guidelines with customization of the available DAR guidelines for national adaptation and dissemination will follow soon after our more comprehensive data is available.
3. Diabetic foot guidelines will be developed after finalization of the local data. At present using the IWGDF document developed in May 2015 with active participation of faculty of Baqai Institute of Diabetology and Endocrinology. We also represented Pakistan's perspective in previous international foot guidelines developed in 2007 and 2011.[5]
4. Gestational diabetes mellitus (GDM) guidelines will be developed by the GDM advocacy board. The advocacy board includes Prof. Zahida Baqai, Prof. Noorjahan Samad, Prof. Abdul Basit, Prof. Shabeen Naz Masood, Dr. Musarrat Riaz, Dr. Asmat Nawaz, Dr. Shehla Naqvi and Mr. Shokat Ali Javed. This advocacy board will develop guidelines for GDM after the completion of two major projects screening around 25000 women. The results for these projects are expected to be available by 2018. This advocacy board will develop guidelines for Gestational diabetes mellitus after screening 25000 women and a registry system will be introduced.

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CHAPTER 02

FACTSHEET

2.1 Objectives

2.2 Definition

2.3 Classification

2.4 Diagnostic Criteria

2.5 Glycaemic Targets

2.1 Objectives:

1. Development of national guidelines for the management of diabetes with limited resources.
2. Development of referral guidelines to and from primary to secondary and tertiary care levels.

2.2 Definition:

Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

2.3 Classification:

Diabetes can be classified into four clinical categories:

1. Type1 diabetes – occurring due to b-cell destruction, usually leading to absolute insulin deficiency.
2. Type2 diabetes – occurring due to a progressive insulin secretory defect and insulin resistance.
3. Gestational diabetes mellitus (GDM) - diabetes diagnosed during pregnancy.
4. Other specific types of diabetes due to other causes, e.g., genetic defects in b-cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug-or chemical-induced diabetes such as during the treatment of HIV/AIDS or drug treatment after organ transplantation

2.4 Diagnostic Criteria:[1-7]

- Diabetes can be diagnosed on the basis of any of the following World Health Organization (WHO) criteria:
- Fasting plasma glucose: ≥126 mg/dl (≥ 7.0 mmol/dl) - Fasting defined as no caloric intake for minimal 8 hours, or
- Random plasma glucose: ≥200 mg/dl (11.1 mmol/l) in the presence of symptoms or
- Plasma glucose after 75 gm glucose load ≥ 200 mg/dl (11.1mmol/l) (Table-I) (Modified oral glucose tolerance test.

Diagnostic Criteria

	Normal (mg/dl)	*IFG/IGT(mg/dl)*	*Diabetic(mg/dl)*
FBS	<110	110-125	>126
RBS/75 gm OGTT	<140	140-200	>200

The above mentioned tests should be performed in laboratory.

***** Asymptomatic individuals with a single abnormal test should have the same test repeated to confirm the diagnosis. On the other hand, if a patient has discordant results in two tests, the test result that is above the diagnostic cut point should be repeated. Symptomatic individuals do not need repetition of the abnormal test.

***** International bodies are now recommending HbA1c as diagnostic criteria but regional/national studies are required before it can be included in national guidelines.[8]

* Population based screening for diabetes may be done using Risk Assessment of Pakistani Individuals for Diabetes (RAPID) scoring system. High risk individuals are advised for laboratory testing.[9]

RAPID (Risk Assessment of Pakistani Individuals for Diabetes)

Risk Factors	*Score***
Age 40-50	1
Age > 50	3
Waist circumference > cut offs*	2
Family History of Diabetes	1

*cut offs are >80 cm in women and >90 cm in men.
**people scoring 4 or more than 4 points should have biochemical tests.

2.5 Glycaemic Targets[10]

Sub Category	*Fasting blood sugar FBS mg/dl*	*Random blood sugar RBS mg/dl*	*Bed time sugar mg/dl*	*HbA1c %*
Recent/without complications	80-120	80-160	100-140	6.5-7.0
With CCF*,CKD†, CLD‡, Autonomic Neuropathy	80-160	120-180	120-180	7.0-7.5

* Congestive Cardiac Failure † Chronic Kidney disease ‡ Chronic Liver disease.

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CHAPTER 03

REFERRAL CRITERIA FOR DIFFERENT LEVELS OF CARE

3.1 Primary Care

3.2 Secondary Care

3.3 Tertiary Care

3.1 Primary Care

Primary physician is the first level of contact for individuals, families and communities, with the health care system. Primary health care facility for people with diabetes shall preferably be offered by certified diabetes doctors and educators. Diabetes educators are an essential part of primary care level.

1. Proper record maintenance for all people with diabetes attending the primary care clinic is advisable. (Proforma 1)
2. Screening for complications of diabetes should be done at first visit and should be repeated at appropriate intervals, and depending upon the progression of disease (details mentioned below).
3. A urine detailed report test should be performed. If proteinuria is present, other causes of proteinuria like urinary tract infection, renel calculi, recent fever or exercise etc should be excluded. The test should be repeated within three months. If it is negative for proteins, test for urinary microalbuminuria is recommended (urinary dipstick for micral test).

   In case of presence of macroalbuminuria, referral should be made to secondary care for further evaluation.[1-8]
4. If serum creatinine level is ≥ 1.5mg/dl, referral to secondary care ought to be considered for further evaluation.
5. The patient should be referred to an ophthalmologist for a comprehensive eye examination on the first visit and at least annually thereafter. The patients with an eye emergency should be referred to ophthalmologist immediately.[9]
6. Foot examination should be carried out and foot care advice should be given to all patients (see chapter 9).
7. Patients presenting with "Feet at Risk" and/or diabetic foot ulcers should be referred for management and/or evaluation.[10] (Table-3 page)
8. Acute swollen painful and/or hot limb /limbs need urgent referral.
9. Diabetic patients with other chronic illnesses like tuberculosis, leprosy, hepatitis B or C, cardiovascular disease and secondary hypertension et, should be directed towards secondary/ tertiary care for comprehensive management.
10. If there is recurrent severe hypoglycemia, the patient should be referred to secondary care level for thorough assessment.
11. Referral should be considered for uncontrolled diabetes, hypertension (BP≥140/90 mm of Hg) or dyslipidemia despite optimal management over a period of 3-6 months.
12. Patients presenting with sudden onset of limb weakness or painful neuropathy unresponsive to first line therapy or patients having signs and symptoms of autonomic neuropathy should be referred.

3.2 Secondary care

The secondary care comprises of multidisciplinary team supervised by a physician having postgraduate qualification or specialized training in diabetes care. The team includes qualified diabetes educators and diabetic foot care assistants.

1. Proper record maintenance for all people with diabetes attending the secondary care clinic is advisable (ideally electronic) (proforma 2)
2. For initial assessment of proteinuria, protocol discussed in primary care level should be followed. For the patients with a positive dipstick test (1+ or greater) proteinuria should be confirmed by a quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio) within 3 months. Patients with two or more positive quantitative tests temporally spaced by 1 to 2 weeks should be diagnosed as having persistent proteinuria and undergo further evaluation and management for chronic kidney disease. If this facility is not available low dose ACE Inhibitors or ARBs may be considered even if blood pressure is within normal range. These patients should be referred to tertiary care centers.[11-15]
3. The patients should be referred for a comprehensive eye examination by an ophthalmologist on first visit, and annually thereafter or according to the advice of the ophthalmologist. An eye emergency should be referred to ophthalmologist immediately.[9]
4. Comprehensive foot examination should be carried out on first visit. Foot care advice should be given to all patients. Identified "Feet at Risk" or patients presenting with foot ulcers should have prompt management.[15] Ulcers not responding to extensive management or showing signs of deterioration at any stage and the subjects for vascular surgery or amputation should be referred to a specialized tertiary care foot care clinic.
5. An ECG should be performed in all patients and referral to tertiary care shall be considered if significant changes are present.
6. Patients with other chronic illnesses like tuberculosis, leprosy, hepatitis B or C, chronic heart failure, ischemic heart disease or angina and secondary hypertension etc should be directed towards tertiary care if comprehensive management for these conditions is not available at secondary level.[16]

3.3 Tertiary Care

Tertiary care level is a university based teaching hospital comprising of an outpatient and inpatient integrated care along with research and education programs. Routine integrated care involves the patient, physician (Professor, Associate Professor, Assistant Professor) with special interest in diabetes, clinical nurse specialist/educators trained in diabetes, dietitians, diabetic foot care assistants and/or podiatrists. Ideally this setup should have necessary disciplines available such as, cardiology, nephrology, ophthalmology, dentistry, psychiatry, orthopedic surgery, vascular surgery, gynaecology and obstetrics etc, providing care for all aspects of diabetes and its complications from prevention to rehabilitation. Any condition that requires more specific intervention should be directed towards more specialized centers.

PROFORMA 1

Clinic Code: _____ Date: _____

Name: _____ Age: _____ Gender: _____

Marital Status: _____ Occupation: _____ Urban/Rural: _____

Patient contact information:

Landline Number: _____ Mobile Number: _____ Email:_____

Family history of: _____

a- Diabetes _____ b-Hypertension _____ c- IHD _____

Type of diabetes: Type 1 /Type 2/ GDM Date of Diagnosis: _____

Any significant past history: _____

Any diabetic complication present: _____

Neuropathy: _____ Retinopathy: _____ Nephropathy: _____

PVD: _____ CVA: _____ MI: _____

Anthropometric Measurement

Height: _____ Weight: _____ BMI: _____

Waist circumference: _____

PROFORMA 1		
Tests	*Date*	*Results*
FBS (mg/dl)		
RBS (mg/dl)		
HbA1c (%)		
Serum Creatinine (mg/dl)		
Total Cholesterol (mg/dl)		
HDL (mg/dl)		
TGs (mg/dl)		
LDL (mg/dl)		
Urine D/R		

Current Medications	
1.	6.
2.	7.
3.	8.
4.	9.
5.	10.

PROFORMA 2

Diabetic Clinic

Name: _____ Age: _____ Computer No: _____

Date	Weight	
HbAIC	Glucose	
Treatment		

Date	Weight	
HbAIC	Glucose	
Treatment		

Date	Weight	
HbAIC	Glucose	
Treatment		

Date	Weight	
HbAIC	Glucose	
Treatment		

PROFORMA 2

Diabetic Clinic Investigation

F.B.S								
R.B.S								
HbA1c								
S.Creatinine								

URINE D/R	
MICRO ALBUMIN	
24hr. U.PROTEINS	
24hr. CCT	

Total LIPIDS								
CHOLESTROL								
TRIGLYCERIDES								
LDL/HDL								

ECG/ETT	
ECHO	

X-RAY CHEST/FOOT

T3, T4, T.S.H

Miscellaneous	

PROFORMA 2

Diabetic Register

Personal Data

Computer Code: _____ Entry Date: _____

Patient Name: _____

Address: _____

Post Code: _____ City: _____

Phone (Res): _____ Phone (Off): _____

Date Of Birth: _____ Age: _____

Reference: _____ Examiner: _____

Gen. Practitioner: _____ Source: _____

G.P Phone: _____

Care Type: _____ Status: _____

Personal History

Year Diagnosed: _____ Year Insulin Started: _____

History of Ketoacidosis: _____

No. Live Births: _____ No. Still Births: _____

No. Neonatal Deaths (<wks.): _____ No. Abortion: _____

Occupation: _____

Family History: _____ Mother History: _____

Father History: _____ Sibling History: _____

Children: _____ Smoking Habits: _____

Drinking Habits: _____

B.P. mm/Hg: _____ Year Insulin Started: _____

Weight (kg) : _____ Height (cm): _____ B.M.I: _____

Visual Acuity	:	L	6/
	:	R	6/
Uncorrected	: = 0		
Spectacles	: = 1		
Visual Acuity	:	L	6/
	:	R	6/
Pinhole	: = 2		

PROFORMA 2

		RIGHT	LEFT
EYES			
Registered Blind? (No=0, Partially Sighted=1, Completely blind=2)		0 1 2	0 1 2
Microdots Nil=0, 1-5=1, 6-10=2, 11+=3		0 1 2 3	0 1 2 3
(Retina not visible = 9)		0 1 2 3 9	0 1 2 3 9
Blot Hemorrhages Exudates (hard)		0 1 9	0 1 9
Absent=0, Present=1, Retina not visible=9		0 1 9	0 1 9
Exudates (soft)		0 1 9	0 1 9
Vitreous Hemorrhage		0 1 9	0 1 9
LIMBS: Pulses:(normal=0, diminished=1, absent=2, amputation=9)	Feromal	0 1 2 9	0 1 2 9
	Popliteal	0 1 2 9	0 1 2 9
	Dorsali pedis	0 1 2 9	0 1 2 9
Tibialis posterior		0 1 2 9	0 1 2 9
Sensation:(normal=0, diminished=1, absent=2, amputation=9) Pin Prick		0 1 2 9	0 1 2 9
Vibration Sense		0 1 2 9	0 1 2 9
Reflexes:(normal=0, diminished=1, absent=2, amputation=9)	Knee	0 1 2 9	0 1 2 9
	ankle	0 1 2 9	0 1 2 9

DIABETIC MEDICATIONS

PROFORMA 2

PREVIOUS TREATMENT

DATE START	INSULINE/TABLET TYPES	DATE STOP	INJECTIONS/DAY

CURRENT TREATMENT DATE START _____

Specify Time:

1=Before breakfast 2=Before midday meal 3=Before evening meal 4=Before bed 5=Continuous Otherwise Specify (24 Hour Clock).

TIME	INSULIN/TYPE	UNITS		UNITS
			+	
			+	
			+	
			+	

TIME	TABLET	DOSE (mg)		
				Tick if diet only

OTHER MEDICATIONS

Please specify other drugs that the patient will start or will continue to take from today and important drugs taken previously. There is no need to record dose etc. For drugs, which have been stopped.

DATE START	DATE STOP	NAME OF MEDICATION	DOSE		TIMES/DAY OR PRN
				g mg mcg ml tabs	
				g mg mcg ml tabs	
				g mg mcg ml tabs	
				g mg mcg ml tabs	
				g mg mcg ml tabs	
				g mg mcg ml tabs	
				g mg mcg ml tabs	

PROBLEMS DETAILS

DIABETES RELATED		ACTIVE OR INACTIVE	YEAR ONSET
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	
Y / N		A / I	

Name of patient: _____
Computer No:_____

DIETARY ASSESSMENT

1st VISIT:

Date: _____

BMI = _____ Lipids = _____

Glycaemia Control = _____

Current caloric intake = _____

Calories required = _____

Calories advised = _____

Type of diet advised = _____

Compliances = 5, 4, 3, 2, 1

2nd VISIT:

Date: _____

BMI = Lipids = _____

Glycaemia Control = _____

Current caloric intake = _____

Calories required = _____

Calories advised = _____

Type of diet advised = _____

Compliances = 5, 4, 3, 2, 1

3rd VISIT:

Date: _____

BMI = Lipids = _____

Glycaemia Control = _____

Current caloric intake = _____

Calories required = _____

Calories advised = _____

Type of diet advised = _____

Compliances = 5, 4, 3, 2, 1

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CHAPTER 04

NON PHARMACOLOGICAL MANAGEMENT OF DIABETES

4.1 Lifestyle Modifications

4.2 Diabetes Education

Lifestyle modifications (LSM) are an important and foremost pillar of management of diabetes. Unbalanced eating habits and unsatisfactory physical activity are main contributors in the development of diabetes.[1] LSM not only improves glycemic control but is also helpful in modest and sustained weight reduction which is specifically important in newly diagnosed cases.[2,3]

4.1.1 DIETARY GUIDANCE FOR PEOPLE WITH DIABETES IN PAKISTAN

Focus on diet quality and dietary patterns.

A. Balanced food group intake[4,5]

1. Frequent and excessively large portions of foods having high proportion of fats, sugar, starch and salt (e.g. baked and fried products) must be discouraged.[6]
2. Intake of fish, skimmed milk and yogurt, green leafy vegetables, lemon, carrots, should be encouraged to increase nutrient density of diets
3. Each meal should have food from several food groups particularly, high protein food, fresh or lightly cooked vegetables and fruits
4. In a day, for most adults consuming two servings of high protein foods (e.g. 6 oz meat), 2 servings of foods from milk group (e.g. two cups of milk/yogurt), and five servings of fruits and vegetables (e.g. 1 cup cooked vegetables, 1 cup salad, one seasonal fruit) is essential to provide sufficient protein, minerals and vitamins.

B. Food safety

1. Due to possible impact of diabetes on immunity, gastrointestinal and kidney functions, people with diabetes may face more severe consequences of consuming unsafe food.[7,8]
2. In view of lack of local regulatory controls, based on expert opinion, on food quality intake of freshly cooked/prepared foods of known origin should be strongly recommended for people with diabetes in Pakistan.

C. Number of meals

1. Number of meals should be determined according to person's lifestyle, metabolic status and medical treatment options. For example, frequent small meals could help in sustaining normoglycemia and preventing hyperphagia in persons having insulin resistance and hyperinsulinemia.

D. Energy and nutrients

1. Energy

- If feasible, energy requirement should be calculated individually for each subject using

  BMR estimation equations and incorporating activity level and stress factor. This can be done using energy estimation calculators.

- In case it is not feasible energy requirement could be based on the basis of ideal body weight (IBW).

  For adults, energy intake could be in the range of 25 to 30 calories per kg of adjusted body weight (i.e. IBW+.25*excess weight). It has been found that in terms of glycemic control, 30kcal/kg IBW was more acceptable energy level for obese person with diabetes.[7,9,10]

2. Protein

- Adequate protein intake is important for controlling metabolic derangements, attaining normoglycemia, preventing muscle loss and maintaining health and well being.
- In Pakistani people with diabetes, protein intake has been found to be inadequate, so for most people increasing its quantity and quality needs to be recommended.
- For adults protein requirements range from 0.8 to 1.2 gram per kg body weight.
- Person getting most of their proteins from vegetable sources need relatively higher amounts of proteins.
- Total protein intake in general and animal protein intake in particular should be distributed in different meals.
- In person having wheat as staple food and having difficulty in taking animal proteins or variety of vegetable proteins, lysine supplement could help in improving protein quality of diet.

3. Proportion of Fats and Carbohydrates

- Recent recommendations do not suggest any particular proportion of calories from fats or carbohydrates.[11] Use of fats and foods high in carbohydrates (e.g. sugars and refined food from the cereal group) should be controlled according to energy requirements.

Carbohydrates

1. Monitoring the total daily carbohydrate intake (by carbohydrate exchanges) is the primary strategy in achieving glycemic control.
2. The total amount of carbohydrate intake is the predominant factor in controlling the post prandial blood glucose level.
3. Meal plan with portion control and individualized diet plan is ideal. Observing the amount of carbohydrates matching with available insulin is the main strategy for good postprandial control.
4. People with diabetes should deduct their CHO intake in form of rice and roti gradually to reduce their weight and improve their glycemic control.
5. Carbohydrate intake (fruits, milk yogurt and starchy food) ideally should not be consumed together.
6. Consistency in carbohydrate intake results in improved glycemic control thus education for carbohydrate counting / estimation must be provided
7. For person taking insulin or insulin secretagouges it is essential that they monitor and control carbohydrate content of their food to prevent severe hypoglycemia. For good health, carbohydrate intake from vegetables, fruits, whole grains, legumes, & dairy products are advisable.
8. People with diabetes and those at risk for diabetes should limit or avoid intake of sugar-sweetened beverages (from any caloric sweetener including high-fructose corn syrup and sucrose) to reduce risk for weight gain and worsening of cardiometabolic risk profile.
9. As carbohydrate intake (in form of roti, snacks, sugar, sweets etc) is in general high in Pakistan, decreasing its intake should be focused.

D. Fats

1. Use of transfats (ghee, margarine) should be firmly discouraged.
2. Use of food containing high amounts of saturated fats specially palm oil needs to be limited
3. Use of oils rich in mono and polyunsaturated fats e.g. mustard oil, canola oil, and corn oil in moderate amounts should be encouraged.

4. Intake of omega 3 fats (from fish, flax seed etc) to balance intake of n3/n6 fatty acids (present in vegetable oils) should be suggested.
5. Use of oils high in monounsaturated fats (e.g olive oil) in place of refined carbohydrates could be recommended as it is cardio protective and helps in glycemic control
6. As fat intake (in form of fat in curries, fried snacks, fat as topping on foods etc) is in high in many regions of Pakistan, decreasing its total intake should be focused.

Physician Delivered Nutrition Therapy Algorithm

A physician delivered nutrition counseling algorithm shown to be effective in primary care settings includes five steps

a. Address the agenda. to the patient to clarify need for nutrition counseling
b. Assess patient's motivation, past diet experience and current diet
c. Advice "Based on your health risks and current diet, we recommend that we focus on (high fat intake, excess calories, inadequate intake of fruits and vegetables)."
d. Assist Negotiate a plan including two or three simple and specific dietary goals, addressing possible barriers and ways to handle them. Determine whether the patient needs additional information or help; refer to dietician as needed
e. Arrange frequent follow-up, either by phone contact, email or return visit.[11]

4.1.2 Physical Activity

Any bodily movement produced by skeletal muscles requiring energy expenditure is called physical activity (PA).[12] PA includes regular movements such as walking, structured exercise such as running, swimming or cycling and weight training exercises.[13] PA is an effective intervention in improving glycaemic control, the main objective in management of type2 diabetes, with an average reduction in HbA1c of 0.6% to 0.79%.[14] Simplest form of PA like 30min walk 5 days a week can result in significant benefits in metabolic control, energy expenditure, better work capabilities, feeling of well being and improvement in cardiovascular risk.[15] A willing patient who is tolerating initial aerobic exercises may also be offered resistant training exercises. These can improve lean body mass thus increasing insulin sensitive tissues.[16] Simple walk with moderate intensity is safe in majority of the people.

Advising PA of greater intensity requires careful history taking and evaluation for presence of any co morbidity.[17] People with proliferative retinopathy or severe non proliferative retinopathy should be advised simple walk. People with compromised visual acuity should be supervised during walk.

Presence of autonomic neuropathy may increase the risk of postural hypotension, decreased cardiac responsiveness to increasing need of cardiac output or hypoglycemic unawareness. In such cases commence with low intensity and duration, gradually increasing to tolerable levels. Peripheral neuropathy leading to feet at risk should be evaluated.[18] If present, moderate intensity walk with appropriate footwear is advisable. Initiating PA may acutely raise proteinuria but it does not lead to progression in nephropathy.[19]

- If people with diabetes have not been active at all, start slowly and increase activity over a period of time. Simple walk for at least 30 min, 5 days a week is enough in initial phases or simple aerobics that increase heart rate 60-70% of maximum (Maximum Heart Rate = 220 - age in years).
- In addition to walk, PA can be increased later on both in duration and intensity (210min/week of simple aerobics or 125 min/week of resistant exercises based on weight training).
- In willing people without any contraindication, structured exercises like running, swimming or cycling can also be introduced.
- Households like mobbing, gardening, laundry etc should also be encouraged to enhance active hours in a day.
- Minimal but significant changes in lifestyle like using stairs instead of taking elevators, parking car at a distance from workplace, keep walking while conversing on phone etc can bring significant change in activity status of a person.
- People should be educated about hypoglycaemia and its management. People requiring insulin or those on sulphonylureas need to be aware of potential delayed hypoglycaemia 6–12 hours after cessation of the PA. A quick glucose source should be kept available during exercise.
- Proper warm up and cool down is advised. The people with diabetes should be advised to stop if cardiovascular symptoms like chest pain or unusual breathlessness develop.
- People with intermittent claudication should be encouraged to continue as these symptoms will improve with time.
- Plenty of water should be taken to avoid dehydration. In extreme weathers indoor alternative exercises are favored.
- People should be advised to examine their feet for any redness, blister or any sign of irritation after exercise. Properly fitting socks and shoes should be worse during exercise.

4.2 Educating People with Diabetes:

Diabetes education is the most important element of management.[20] The continuing management of diabetes requires the person living with it to self-manage and should be able to make simple decisions regarding meals, exercise and medications. It is also significant that people with diabetes should be able to do self monitoring of blood glucose, examination and care of feet and recognition and correction of hypoglycaemia.[21,22] Diabetes education should be commenced at the time of diagnosis and frequent follow ups are advisable for adherence.

4.2.1 Hypoglycaemia

Hypoglycaemia is defined as blood glucose level less than 70 mg/dl.[18] The symptoms associated with it are due to neuroglycopenia. Recognizing hypoglycaemia is important so that steps can be taken to prevent a medical emergency. Symptoms include trembling, sweating, palpitation, change in vision, hunger, headache, mood swings, behaviour changes, lack of coordination, inattention and confusion. When severe, seizures and loss of consciousness may occur. Sometimes people with diabetes treated with insulin or insulin secretagogues lose their ability to identify hypoglycaemia, a condition known as hypoglycaemic unawareness.

This is due to repeated hypoglycaemic episodes that reprogram trigger center for release of stress hormones at even lower blood glucose level. These stress hormones not only help to combat hypoglycaemia but also trigger symptoms for awareness, hence making patient unaware of the condition. Hypoglycaemic unawareness can be managed by keeping the blood glucose above the normal range for few weeks and avoiding hypoglycaemic events. Frequent monitoring is advised in this condition and targets for glycaemic control might need to be redefined.

4.2.2 Hyperglycaemia

High blood glucose levels can lead to acute presentation like hyperosmolar hyperglycaemic state or chronic micro or macro vascular complications. Regular blood glucose testing is helpful as people with diabetes often do not feel symptoms. Short-term symptoms of high blood glucose include polyuria, polydipsia, nocturia, blurred vision, non healing ulcers and fatigue. A number of conditions or factors can contribute to hyperglycaemia. Lack of proper PA, taking carbohydrate rich food more than usual without adjusting insulin or medicines, any illness or psychosocial problem leading to excessive stress and forgetting or intentionally skipping medicines or insulin are common contributing factors. Detailed history along with assessment of behavior is essential to correctly diagnose the reason. Self monitoring of blood glucose should be emphasized and possible intensification of medicines or insulin may be done.[22]

4.2.3 Self monitoring of blood glucose

The required frequency of monitoring should be advised in accordance to the scenarios discussed in BRIGHT recommendations. Adherence to this frequency should be emphasized whenever possible.[23]

BRIGHT Recommended SMBG

Table 1 : Lowest Intensity

Twice Weekly
Days and timings are variable

	Breakfast		Lunch		Dinner		Bed Time
	Pre	Post	Pre	Post	Pre	Post	
Mon	✓						
Tue							
Wed							
Thu							
Fri						✓	
Sat							
Sun							

- Controlled non affording type 2 diabetics
- Women with controlled gestational diabetes on lifestyle modification
- Geriatric patients (aged >70 years) controlled with or without co-morbid conditions.

Table 2 : Moderate Intensity

1-2 Times Daily Depending on control of blood glucose (7-14 points per week)
Days and timings are variable

	Breakfast		Lunch		Dinner		Bed Time
	Pre	Post	Pre	Post	Pre	Post	
Mon	✓				✓		
Tue		✓				✓	
Wed	✓		✓				✓
Thu				✓			
Fri	✓				✓		
Sat		✓				✓	
Sun	✓						✓

- Newly diagnosed or uncontrolled non affording type 2 diabetics
- Controlled affording type 2 diabetics
- Controlled non-affording type 1 diabetics
- Women with controlled gestational diabetes on lifestyle modification
- Geriatric patients (aged >70 years) controlled with or without co-morbid conditions.

Table 3 : High Intensity

4 Times Daily (28 points per week)
Days and timings are variable

	Breakfast		Lunch		Dinner		Bed Time
	Pre	Post	Pre	Post	Pre	Post	
Mon	✓		✓		✓		✓
Tue	✓	✓		✓		✓	
Wed	✓	✓			✓		✓
Thu	✓		✓	✓		✓	
Fri	✓	✓			✓	✓	
Sat	✓		✓	✓			
Sun	✓		✓		✓	✓	✓

- Newly diagnosed or uncontrolled affording type‡ 2 diabetics
- Newly diagnosed or uncontrolled non affording type 1 diabetics
- Controlled affording type 1 diabetics
- Women with controlled gestational diabetes on insulin
- Pre-operative care (duration of 1 week)

Table 4 : Intensive SMBG

4-6 Times Daily (28 - 42 points per week)
Days and timings are variable

	Breakfast		Lunch		Dinner		Bed Time
	Pre	Post	Pre	Post	Pre	Post	
Mon	✓		✓		✓		✓
Tue	✓	✓		✓	✓	✓	
Wed	✓	✓		✓	✓		✓
Thu	✓	✓	✓	✓	✓	✓	
Fri	✓	✓	✓		✓		✓
Sat	✓	✓	✓	✓	✓		✓
Sun	✓		✓	✓	✓	✓	

- Newly diagnosed or uncontrolled affording type 1 diabetics
- Type 2, type 1 or gestational diabetes with inter-current illness or hospitalization
- Women with controlled gestational diabetes on insulin

4.2.4 Signs and Symptoms of Foot Problems

People with diabetes should be educated about warning signs of foot problems and daily foot care (see chapter 9).

4.2.5 Sick Day Rules

People with diabetes should be educated about sick days and common illnesses like flu, fever, sore throat, diarrhea, vomiting, urinary tract infection or any other such ailment. Sick Day Rules

1. Self monitoring of blood glucose should be frequent 4-6 points/day.
2. Early physician advice should be sought regarding all medicines.
3. Plenty of water, fresh juice with pulp or soup should be taken. Avoid sugary or caffeine containing drinks.
4. Refer for hospitalization if symptoms persist for more than six hours or in case of uncontrolled blood glucose levels.

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CHAPTER 05

PHARMACOLOGICAL MANAGEMENT OF DIABETES

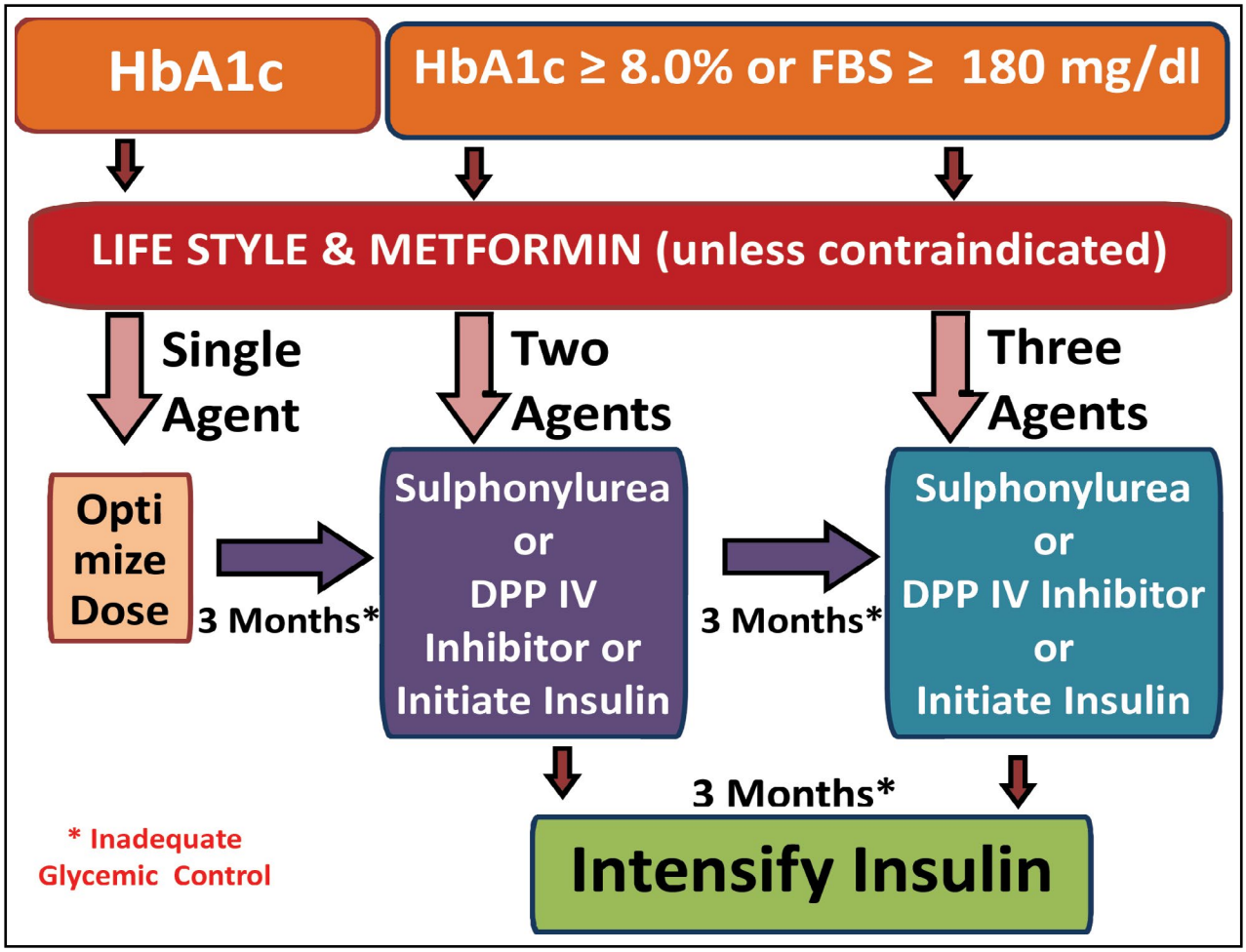
5.1 Overview:

1- Any of the selected regimes should be evaluated every three months with HbA1c and SMBG. If HbA1c is not available, SMBG and/or lab records can be helpful. People with diabetes should be assessed for possible side effects of drugs including hypoglycemic events, weight gain, fluid retentions, hepatic or renal impairment or cardiovascular risks. They should also be assessed for co morbidities, drug adherence and psychosocial issues.[1]

2- Modifications in lifestyle like alterations in dietary habits specially aiming to reduce weight in overweight or obese persons, increase in PA and smoking cessation are most important and initial steps in the management of type 2 Diabetes.

3- Metformin should be prescribed to all patients along with lifestyle modifications, irrespective of their baseline BMI, if there are no contraindications.[2-8] If metformin is contraindicated or is not tolerated, DPP4 Inhibitors, sulphonylureas or insulin can be used as alternative.[9]

4-In newly diagnosed people with diabetes presenting with signs and symptoms of hyperglycaemia or having HbA1c >8.5%, a second oral agent or insulin should be considered along with metformin.[10-22] Initial combination of sub maximal doses of antihyperglycaemic agents produces better and quicker response than maximum doses of monotherapy.[23,24]



Factors Influencing Management Strategies

CLINICAL FACTORS

* Age of Individual
* Weight of Individual
* Degree of Hyperglycaemia/hypoglycaemic unawareness
* Risk of Hypoglycaemia
* Presence of any comorbidity/ complication
* Socio-Economic Status
* Individual Preference

PHARMACOLOGICAL FACTORS

* Efficacy in Glycaemic Control
* Risk of Hypoglycaemia
* Risk of Weight gain
* Drug interactions
* Side Effects
* Cost and Availability

5.2.1 Oral Hypoglycemic Agents

Metformin

- Metformin (dimethylbiguanide) is currently the drug of first choice for the treatment of hyperglycaemia associated with diabetes mellitus without stimulating insulin secretion, promoting weight gain, or causing hypoglycaemia.[25]
- Metformin is an insulin-sensitizer, which causes reduction in insulin resistance and a significant decrease in plasma fasting insulin levels. Metformin monotherapy can reduce HbA1c by 1.5%.[26]
- It also provides benefits of weight stability or slight weight reduction.[27]
- It is generally well tolerated. Most commonly reported side effects are anorexia, nausea, diarrhea and metallic taste. These effects can be minimized if metformin is taken with meals.
- Lactic acidosis is the only serious side effect. However its risk incidence is extremely low[28,29]
- It is contraindicated in end stage renal failure (eGFR<30).[30] If eGFR is not available metformin should be discontinued at serum creatinine >1.5mg/dl.
- Metformin is excreted by the kidney. The reduction in renal clearance of metformin is considered as an important risk factor for lactic acidosis.[31] It should be started in low dose and titrated upwards until the required glycemic targets are achieved or another oral agent is added in regime.[1-6]
- It may also be associated with B12 deficiency in some cases with long term use.[32]
- The maximum dose is upto 3000 mg in divided doses. It should be started with low dose typically 500mg twice daily with upward titration if desirable control of hyperglycaemia is not achieved. The drug is well tolerated.

Sulphonylureas (SU)

SUs reduce plasma glucose levels by enhancing insulin secretion, with an average HbA1c reduction of 1.5%.[33]

- The major adverse side effect is hypoglycaemia. The risk is higher in renal impairment, liver cirrhosis and in the elderly. Weight gain is also a common side effect.[34]
- Second generation SUs (gliclazide, glimepiride) cause less risk of hypoglycaemia and less weight gain.
- SUs are highly protein bound. Administration of drugs like non-steroidal anti-inflammatory drugs (NSAIDs), antithyroid drugs, sulpha drugs, anticoagulants and α-blockers) can displace them increasing the risk of hypoglycaemia.[35]

Dipeptidyl Peptidase IV (DPP-4) inhibitors (DPP4 Inhibitors)

- The oral dipeptidyl peptidase IV (DPP-4) inhibitors or incretin enhancer increase circulating concentrations of active GLP-1 and GIP.[36]
- DPP-4 inhibitors lower HbA1c by approximately 0.6-1.0% and are weight neutral.[37]
- DPP-4 inhibitors have proven efficacy when combined with metformin, sulfonylurea or both metformin and sulfonylurea.

- They carry low risk of hypoglycaemia.
- Furthermore, recent cardiovascular studies with DPP-4 inhibitors have shown that these agents do not increase the CV risk.[38-42]

Alpha glucosidase inhibitor

- The digestion of carbohydrates including starch and table sugar is prevented by alpha glucosidase inhibitor (GI) thus controls postprandial hyperglycaemia.[43]
- It can reduce HbA1c by 0.2%.[44]
- Its major side effects are bloating and flatulence. Hence usually not well tolerated.[45] Side effects can be avoided by slow titration of dosage.

GLP 1 agonists

- The incretin hormone glucagon-like peptide 1 (GLP-1) is known for the 'incretin effect'.
- They facilitate insulin release in state of hyperglycaemia.[46]
- They also suppress pancreatic glucagon output, retard gastric emptying and diminish appetite. This usually results in weight reduction.
- These are expensive and administered subcutaneously on daily basis.
- They can reduce HbA1c by 1.1%.[47]

Thiozolidinedione (TZDs)

- These insulin sensitizers are PPAR gamma agonist.
- The major side effects include edema, weight gain, risk of congestive heart failure (CHF) and increased risk of fractures. This significantly limits their clinical use.[48-50]
- They have conflicting findings regarding myocardial infarction (MI) risk. However, they should not be used in NYHA class 2 patients.[51,53]
- Inconclusive evidence is present for their association with bladder cancer.[54]

Repaglinide

- It is relatively short-acting stimulators of insulin secretion (<6 hours).
- They act by binding to ATP dependant potassium channels on pancreatic beta cells.[55]
- The main risk is hypoglycaemia and weight gain.[56]
- Repaglinide is mainly excreted through hepatic route hence is safe in renal compromised patients.[55]

5.2.2 INSULIN

- It can be categorized according to either duration of action ranging from rapid acting insulin to short acting, intermediate acting, long acting and very long acting insulin or their source as human or analogue insulin.
- The human insulin is less expensive than analogues, hence more affordable.
- The dose should be adjusted at regular intervals. Less expensive human insulin are beneficial in most of the cases particularly if comprehensive education about preventing, identifying and timely correction of hypoglycemia has been imparted.
- Different types of insulin and their duration of action are discussed in the table given below.

Types of insulin	*Available strengths*	*Onset of action*	*Peak action*	*Duration of action*	*Physical app.*	*Combinations*
Human Insulin						
Regular		30-60 min	2-4 hrs	5-7 hrs	clear	NPH
NPH		1-2 hrs	6-14 hrs	12-24 hrs	cloudy	Regular
Regular/NPH premixed	70/30,	30	2-12	24	cloudy	-
Analogues						
Rapid acting insulins						
Insulin Aspart		10-20 min	1-3 hrs	3-5 hrs	clear	NPH
Insulin Glulisine		15-30 min	30min-90 min	3-5 hrs	clear	NPH
Insulin Lispro		15-30 min	30min-90 min	4-5 hrs	clear	NPH
Long acting insulins						
Insulin Detemir		90 min	peakless	upto 24 hrs	clear	
Insulin Glargine		90 min	peakless	upto 24 hrs	clear	
Aspart Protamine suspension	50/50, 70/30	10-20 min	1- 3.75hrs	upto 24 hrs	cloudy	
Lispro Protamine suspension	50/50, 75/25	15-30 min	30min - 2.5hrs	14- 24 hrs	cloudy	

Generic names	**Available strengths**
Regular insulin	
NPH	
Regular/NPH premixed	70/30
Insulin Aspart	
Insulin Glulisine	
Insulin Lispro	
Insulin Detemir	
Insulin Glargine	
Aspart Protamine suspension	30/70, 50/50
Lispro Protamine suspension	75/25, 50/50

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CHAPTER 06

ACUTE EMERGENCIES IN TYPE2 DIABETES

6.1 Hypoglycaemia

6.2 Hyperosmolar Hyperglycaemic State (HHS)

6.1 Hypoglycaemia

It is a common and potentially serious condition which usually occurs as a complication of treatment of diabetes mellitus. It can be classified into mild, moderate and severe according to the severity.

- Mild hypoglycaemia presents with symptoms like trembling, palpitation, sweating, anxiety, hunger and nausea. The individual is able to self-treat.
- Moderate hypoglycaemia presents with neuroglycopenic symptoms like confusion, weakness, drowsiness, changes in the vision and difficulty in concentration in addition to symptoms of mild hypoglcaemia. The individual is able to self-treat.
- Severe hypoglycaemia requires assistance of another person. Unconsciousness may occur. Risk factors include prior history of hypoglycaemia, strict glycaemic control (HbA1c <6.0%), hypoglycaemic unawareness, cognitive impairment and lower socioeconomic status.
- Management is by giving 3 teaspoons of table sugar or honey dissolved in 250ml of water, in the conscious patients. Blood glucose should be retested in 15 min. If it is still less than 70 mg/dl repeat oral ingestion of carbohydrate. Severe episode in an unconscious patient is treated by giving 20-50 cc of 50% dextrose water intravenously in 1-3 minutes.
- The person should have usual meal or snack containing carbohydrate and protein that is due at that time to prevent repeated hypoglycaemia. If meal time is more than an hour away, a snack containing 15 g of carbohydrate such as sandwich, biscuits or half chapatti along with portion of protein should be taken.
- People on medicine which can potentially cause hypoglycaemia should have proper education on prevention, recognition and management of hypoglycaemia.

6.2 HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS)

HHS is associated with significant morbidity and higher mortality than DKA and must be diagnosed promptly and managed intensively.[1-3] The clinical picture is dominated by profound dehydration, without ketosis or significant acidosis. Plasma glucose level usually exceeds 600 mg/dl. If HHS continues, severe dehydration will lead to seizures, coma and eventually death. HHS may take days or even weeks to develop. The warning signs of HHS are dry, parched mouth, extreme thirst (although this may gradually disappear), warm, dry skin that does not sweat, high fever, sleepiness or confusion, loss of vision, hallucinations, weakness on one side of the body and absence of ketosis.

6.2.1 Diagnostic Criteria:

- Plasma glucose level of 600 mg/dl or greater
- Effective serum osmolality of 320 mOsm/kg or greater
- Profound dehydration, up to an average of 9L
- Alteration in consciousness

6.2.2 Management of HHS:

The goals of treatment are to treat the underlying cause and to gradually normalize the osmolality with replacement of fluid and electrolyte losses along with the correction of blood glucose. Other goals include prevention of thrombosis, cerebral edema, foot ulceration and bed sores.

6.2.2.1 Management at Primary Care

Urgently refer to tertiary care. Meanwhile, the infusion of fluid with normal saline should be continued until hospitalization. Four to six units of rapid acting insulin should be administered intramuscularly.

6.2.2.2 Management at Secondary Care

If secondary care provides inpatient facility, manage as tertiary care level, otherwise refer to tertiary care after maintaining intravenous line with 0.9 % normal saline. Maintain intravenous infusion with normal strength saline until dehydration is corrected and urinary out flow is adequate. Fluid losses in HHS are estimated to be between 100 -220 ml/kg.[2] The rate of rehydration will be determined by assessing the combination of initial severity and any pre-existing co-morbidities. Caution is needed, particularly in the elderly, as too rapid rehydration may precipitate heart failure but insufficiency may fail to reverse acute renal injury.[2]

6.2.2.3 Management at Tertiary Care

- Measure or calculate osmolality (2Na+ + glucose + urea) frequently to monitor the response to treatment.
- Use intravenous (IV) 0.9% sodium chloride solution as the principle fluid to restore circulating volume and reverse dehydration. Only switch to 0.45% sodium chloride solution if the osmolality is not declining despite adequate positive fluid balance. An initial rise in sodium is expected and is not itself an indication for hypotonic fluids. The rate of fall of plasma sodium should not exceed 10mmol/L in 24 hours.
- The fall in blood glucose should be no more than 80mg/dl/hr. Low dose IV insulin (0.05 units/kg/hr) should only be commenced once the blood glucose is no longer falling with IV fluids alone or immediately if there is significant ketonaemia (3α-hydroxy butyrate greater than 1 mmol/L or urine ketones greater than 2+).
- Intravenous fluid replacement aims to achieve a positive balance of 3-6 liters by 12 hours and the remaining replacement of estimated fluid losses within next 12 hours though complete normalisation of biochemistry may take up to 72 hours.
- The patient should be encouraged to drink as soon as it is safe to do so and an accurate fluid balance chart should be maintained until IV fluids are no longer required.
- Assessment for complications of treatment e.g. fluid overload, cerebral oedema or central pontinemyelinosis (as indicated by a deteriorating conscious level) must be undertaken frequently (every 1-2 hours).
- Underlying precipitants must be identified and treated.

- Prophylactic anticoagulation is required in most patients.
- All patients should be assumed to be at high risk of foot ulceration if obtunded or uncooperative, the heels should be appropriately protected and daily foot checks undertaken.[3]
- Very rarely type 2 diabetics can present with ketoacidosis. The overall emergency management is as above. Detailed management will be covered in guidelines for management of type1 diabetes to be prepared soon.

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CHAPTER 07

MICROVASCULAR COMPLICATIONS OF DIABETES

7.1 Nephropathy

7.2 Retinopathy

7.3 Neuropathy

7.1 Nephropathy

- Diabetic nephropathy is the leading cause of end stage renal failure. It affects approximately 20-40% of diabetic patients.[1,2] All people with type2 diabetes should be screened annually for presence of microalbuminuria.[3]
- Uncontrolled diabetes or hypertension, fever, infection, recent exercise or congestive cardiac failure may result in protienuria without kidney disease.[4,5] Two readings three months apart should be taken before making a diagnosis of nephropathy.
- If proteinuria is present (30-300mg/day) in two readings a low dose ACE inhibitor or ARB may be started even in normotensive people after taking baseline serum creatinine and potassium.[4]
- If hypertension is accompanying diabetes then first line anti hypertensives are ACEI or ARBs. Combination of these drugs with each other should be avoided due to increase incidence of hyperkalemia.[6] Blood pressure targets shoud be < 140/90. Ref JNC [7]
- Serum creatinine and potassium should be rechecked after 10 days and 6 weeks in cases of newly prescribed ACEI/ARBs. It is common to have an acute rise in serum creatinine of up to 30% within 2 5 days of initiating an ACEI/ARB. These can be safely continued in patients if the creatinine subsequently stabilizes at the higher level.[8]
- Good metabolic control is essential to delay the progression of nephropathy.
- Dietary proteins should be restricted to 0.8mg/kg / day if macroalbuminuria is present.[1]
- If urinary albumin excretion is more than 300 mg/dl refer the patient to secondary care.
- Consider referral to tertiary care if kidney disease is rapidly progressive or in absence of retinopathy to evaluate for other causes of renal disease. Referral is also considered if anemia, resistant hypertension, electrolyte imbalance, any bone disease or secondary hyperparathyroidism is present.[4]

7.2 Retinopathy

- All people with diabetes should have detailed history of any existing eye problem. Refer for dilated eye examination by an ophthalmologist at diagnosis or first visit to the clinic.[8]
- If no sign of retinopathy is present repeat examination annually. If retinopathy is present, frequency of examination should be suggested by ophthalmologis.
- Urgent referral is required in case of rapidly deteriorating vision, severe pain or any other eye emergency.
- Good metabolic control is mainstay of prevention or slow progression of retinopathy.[9]
- It is preferable to screen for retinopathy before initiating insulin.

7.3 Neuropathy

1. All people with diabetes require thorough assessment for peripheral neuropathy on presentation. Frequency of follow up assessment depends on presence of neuropathy and/ or loss of protective sensations. Most common presenting complaints are pain, burning and tingling sensations. Almost 50% of patients may be asymptomatic. Identifying these insensate feet is important for prevention of foot ulcers.[4]

2. This assessment includes testing with 10gms monofilament and any of the additional tests for pin prick, vibration or temperature sense.[4]
3. Optimal control of blood glucose levels may slow the progression of neuropathy.[10]

- Assessment and management of autonomic neuropathy may improve quality of life. It may present clinically with gastroparesis, diarrhea, constipation, fecal incontinence, increased or decreased sweating, orthostatic hypotension (a fall in systolic or diastolic blood pressure by 20 mmHg or 10 mmHg, respectively, upon standing without an appropriate increase in heart rate), resting tachycardia (>100 beats per min), neurogenic bladder and erectile dysfunction. Management of these complaints is symptomatic alongwith good glycemic control.
- Urgent referral is required in case of rapidly deteriorating vision, severe pain or any other eye emergency.
- Good metabolic control is mainstay of prevention or slow progression of retinopathy.[9]
- It is preferable to screen for retinopathy before initiating insulin.

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CHAPTER 08

MACROVASCULAR COMPLICATIONS

8.1 Hypertension

8.2 Peripheral Artery Disease

8.3 Dyslipidemia

8.4 Aspirin

8.1 Hypertension

Hypertension is a common diabetes comorbidity that affects the majority of patients, and is a major risk factor for both CVD and microvascular complications.[1]

8.1.1 Monitoring

- Blood pressure should be measured at every routine visit. Patients newly diagnosed with systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mm Hg should have blood pressure confirmed on a subsequent day.
- Blood pressure measurement should be measured by trained personnel. Standard protocol for blood pressure measurement must be followed i.e, in the seated position, with feet on the floor and arm supported at heart level, after 5min of rest. Cuff size should be appropriate for the upper arm circumference.[2,3]

8.1.2 Goals (Targets)

- Systolic blood pressure (SBP) target should be <140 mmHg and diastolic blood pressure should be <90 mmHg in all people with diabetes and hypertension.[4] There is limited evidence for the benefits of further lowering systolic blood pressure or diastolic blood pressure targets.[5]

8.1.3 Therapeutic Management Strategies

- On diagnosis of diabetes, patients should be evaluated for cardiovascular disease, and its factors.
- Laboratory tests include serum creatinine, electrolytes, lipid profile and quantification of urinary albumin excretion.
- Patients with blood pressure >120/80 mmHg should be advised on lifestyle modification to reduce blood pressure.[6-8]
- Lifestyle modifications consists of restricting sodium intake (2,300 mg/day), reducing 10% excess body weight, increasing consumption of fruits and vegetables (4-5 servings per day), consuming low-fat dairy products (2–3 servings per day)[6,8] and increasing activity levels.[7]
- Patients with confirmed blood pressure readings of >140/90mmHg should be promptly initiated pharmacological therapy, in addition to life style modifications. Therapy must be titrated to achieve the desired goals.
- For patients with diabetes and hypertension, ACE inhibitor/ARBs should be considered as initial therapy.[8-11]
- If target blood pressure level is not achieved after 2-3 months, addition of either a ß-blocker or calcium channel blocker or thiazide diuretic may be considered.
- For initial blood pressure >150/100mmHg, a second agent like ß-blocker or calcium channel blocker or thiazide diuretic shall be given along with ACE inhibitor orARB.[12]
- Achievement of target blood pressure level is critical. Multiple-drug therapy (including a thiazide diuretic and ACE inhibitor/ARB, at maximal doses) is generally required to achieve blood pressure targets.

- If ACE inhibitors, ARBs, or diuretics are used, serum creatinine and serum potassium levels should be monitored at 10 days and 6 weeks. Ideally monitor creatinine every six to twelve months if it does not exceed more than 30% from its baseline.[13]
- It is common to have an acute rise in serum creatinine of up to 30% within 2-5 days of initiating an ACEI or ARB, especially if the patient has CKD/CHF. These can be safely continued in these patients if the creatinine subsequently stabilizes at the higher level.[13]
- If blood pressure remains uncontrolled despite good compliance to optimal doses of at least three antihypertensive agents of different class, one of which should be a diuretic, an evaluation for secondary hypertension should be considered.
- In pregnant patients with diabetes and chronic hypertension, blood pressure targets of 110–129 / 65–79 mmHg are suggested. ACE inhibitors and ARBs are contraindicated during pregnancy.[14] Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, diltiazem, clonidine, and prazosin.[15]

8.2 Peripheral Artery Disease

8.2.1 Introduction:

Peripheral artery disease (PAD) is defined as any atherosclerotic arterial occlusive disease below the level of the inguinal ligament resulting in a reduction in blood flow to the lower extremity. Identifying PAD among patients with foot ulceration is important because its presence is associated with worse outcomes, such as a slower (or lack of) healing of foot ulcers, lower extremity amputations, subsequent cardiovascular events and premature mortality.[16-18]

8.2.2 Diagnosis and Treatment:

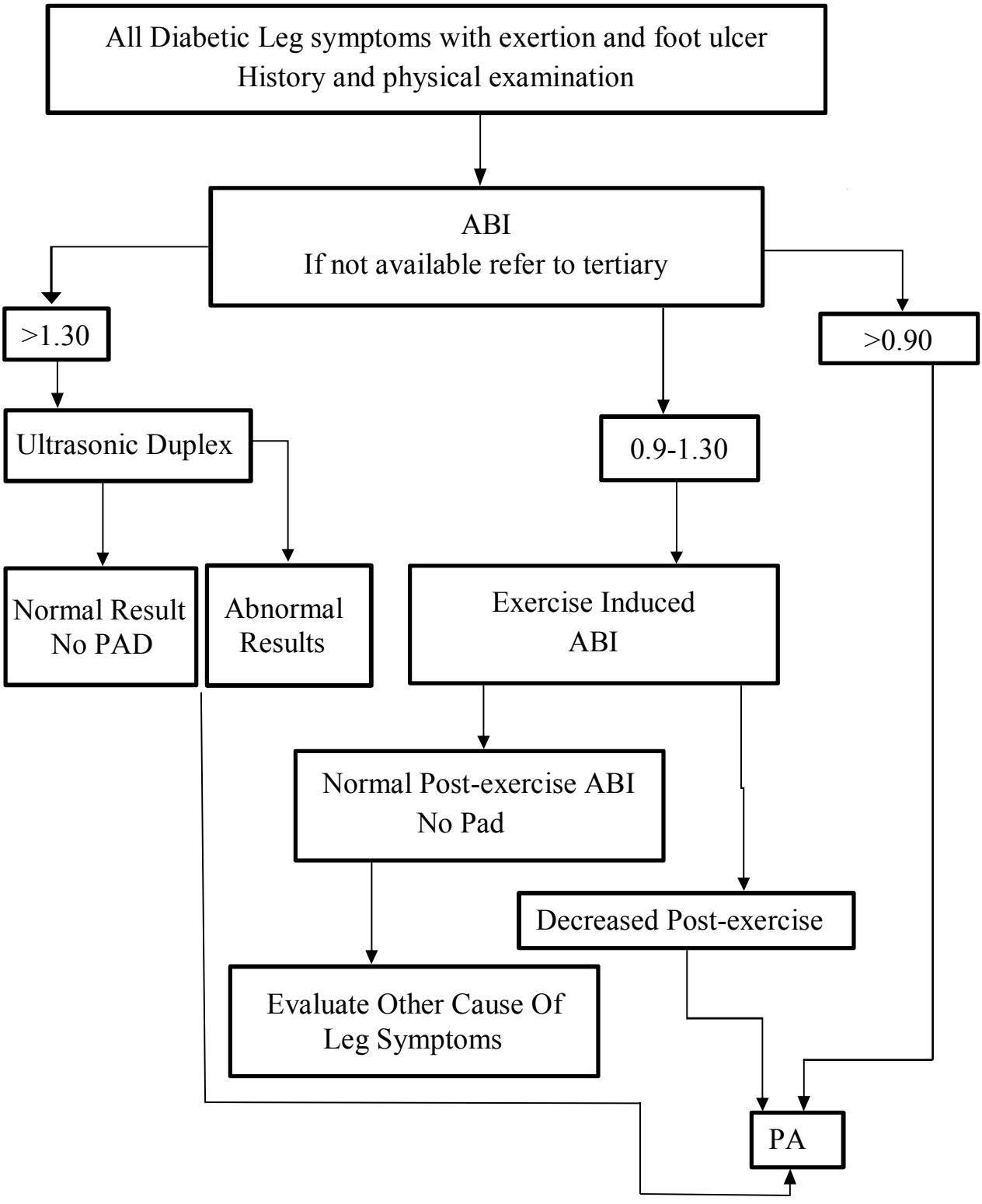
1. Examine a patient with diabetes annually for the presence of PAD; this should include at least taking a history and palpating foot pulses.[19]

2 ABI is an appropriate measurement for the detection of PAD. The ABI is defined as the ratio of the ankle systolic blood pressure divided by the brachial systolic blood pressure, and is normally between 1.0 and 1.3.[20,21] In PAD, the ankle systolic blood pressure is less than the brachial systolic blood pressure, and the ABI is <0.9. Lower ABI values indicate more severe PAD and a higher risk of cardiovascular events.

3 The exclusion of patients with incompressible arteries as defined by an ABI ≥1.[22,23] In such cases other non invasive method like Doppler ultrasound is advised.

4 All diabetic patients with non healing ulcer having ABI <0.9 should be referred to secondary or tertiary centers for further evaluation of PAD by color duplex ultrasound followed by CT angiography, MR angiography or standard X-ray angiography, if required.

5 All patients with diabetes and an ischemic foot ulcer should receive aggressive cardiovascular risk management including support for cessation of smoking, treatment of hypertension, control of glycaemia and prescription of a statin as well as low-dose aspirin or clopidogrel.[24]


All Diabetic Leg symptoms with exertion and foot ulcer
History and physical examination
ABI
If not available refer to tertiary
>1.30
>0.90
Ultrasonic Duplex
0.9-1.30
Normal Result
No PAD
Abnormal
Results
Exercise Induced
ABI
Normal Post-exercise ABI
No Pad
Decreased Post-exercise
Evaluate Other Cause Of
Leg Symptoms
PA

8.3 Dyslipidemia

- It is a disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. It may be manifested by elevation of the total cholesterol, low density lipoprotein (LDL) cholesterol and the triglyceride concentrations, and/or a decrease in the high-density lipoprotein (HDL) cholesterol concentration in the blood.[25]
- Obtain lipid profile at presentation and annually afterwards for intensification and to monitor the response of management. If lipid profile cannot be obtained at presentation, low dose statin is recommended for both primary and secondary prevention. This approach provides an opportunity for reducing rates of premature cardiovascular events.[26,27] All patients with type2 diabetes over the age of 40 should receive statin therapy, despite any level of baseline LDL, unless a very clear risk is identified to withheld the therapy.[28]
- Lifestyle modifications specially targeting weight reduction in overweight or obese people and modification of diet is the mainstay of management of dyslipidemia. (see chapter 10)
- All the diabetic patients aged > 40 without any other risk factor should be given low dose statin. If other cardiovascular disease risk factors are present consider moderate or high dose statins depending on response to statin therapy, baseline LDL cholesterol and side effects profile.[29,30]
- Statin is the preferred medication. If statin is not tolerated or a particular LDL-C goal is not achieved on statin alone, addition of a nonstatin lipid-lowering agent can be considered.
- Target LDL cholesterol to be lowered by 50 percent of the baseline or less than 100mg/dl. In patients with atherosclerotic cardiovascular disease risk factors LDL cholesterol target <70 mg/dl is advisable.[31]
- If triglycerides are high, more than 150mg/dl but less than 500mg/dl, strict lifestyle modifications, glycemic control and statins are recommended. If triglycerides are more than 500mg/dl in fasting, fibrates can be preferred choice.
- If both triglycerides and LDL cholesterol are raised, target LDL cholesterol first by statins. Combination of statin and fibrate is not recommended as it does not result in significant benefits in respect of improved atherosclerotic cardiovascular disease outcome but have high side effect profile.[32]

8.4 Aspirin therapy

Low dose aspirin therapy is an option in people with diabetes with increased CVD risk. This includes family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria and age more than 50yrs. It may not be recommended in people younger than these ages without additional CVD risk factors. People intolerant to aspirin or if there is any contraindication, clopidogrel is an alternate option.[30]

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CHAPTER 09

DIABETIC FOOT

9.1 Diabetic Foot

9.2 Management of diabetic foot ulcers

9.3 Warning signs of foot problems

9.4 Daily Foot Care

9.1 Diabetic Foot

1. People with diabetes are at increased risk of foot ulcers and amputations. Around 85% of amputations are preceded by ulcers which are preventable.[1] Identify feet at risk by appropriate measures.[2] Following are recommendations for assessment and management of diabetic feet.

Table-I: Risk Classification system and preventative screening frequency.[3]

Category	*Characteristics*	*Frequency*
0	No peripheral neuropathy	Once a year
1	Peripheral neuropathy	Once every 6 months
2	Peripheral neuropathy with peripheral artery disease and/or a foot deformity	Once every 3-6 months
3	Peripheral neuropathy and a history of foot ulcer or lower-extremity amputation.	Once every 1-3 months

2. Annual foot examination to identify the presence of peripheral neuropathy or peripheral artery disease, previous healed ulcers, foot deformity, pre ulcerative signs, improper hygiene or foot wear or any level of amputation is advisable. A risk category should be assigned (Table-I) for further preventive measures. Examination is also essential even in the absence of symptoms Fig-1.
3. Assessment of neuropathy can be done with monofilament for pressure perception, 128 Hz tuning fork for vibration sense and tactile sensation by cotton wool. Achilles tendon reflex should be examined.
4. History of claudication or rest pain in lower limb should be taken. Inspect for color, temperature or oedema. Palpation of pedal pulses at each examination should be done. If symptoms of peripheral disease are present and/or pedal pulses are absent refer the patient to tertiary care.

9.2 Management of diabetic foot ulcers

1. If an ulcer is present, classify it as neuropathic, neuro-ischemic or ischemic by history and clinical examination. The plantar surfaces of the feet or areas overlying a bony deformity are common sites for neuropathic ulcers.
2. Ischemic and neuro-ischemic ulcers are more frequent on the tips of the toes or the lateral borders of the foot.Fig.2 & 3.
3. For appropriate assessment, the neuropathic ulcers with callus and necrotic tissue should be debrided as soon as possible.
4. If it is required, patient should be referred to secondary care center. Debridement should not be performed in non-infected ulcers with signs of severe ischemia.[4]
5. Treatment of ulcer includes good metabolic control, off loading of ulcer site with custom made shoes (Fig.4), debridement and cleaning of all necrotic tissue and antibiotics.
6. Give antibiotic coverage appropriately and for prolong periods.
7. Regular follow up should be done with daily dressings.

8. Proper off loading custom made shoes enhance wound healing. Fig.4

9. Deep ulcers involving bone or requiring abscess drainage or if an ulcer is identified as purely ischemic, refer to tertiary care center where foot care facilities are available.

University of Texas Diabetic Foot Ulcer Classification System.[5]

Stage	*Grade*			
	0	*I*	*II*	*III*
A (no infection or ischemia)	Pre- or post-ulcerative lesion completely epithelialized	Superficial wound not involving tendon, capsule, or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	Infection	Infection	Infection	Infection
C	Ischemia	Ischemia	Ischemia	Ischemia
D	Infection and ischemia	Infection and ischemia	Infection and ischemia	Infection and ischemia

Fig.1: Examination of feet for assessment of neuropathy and paedal pulses

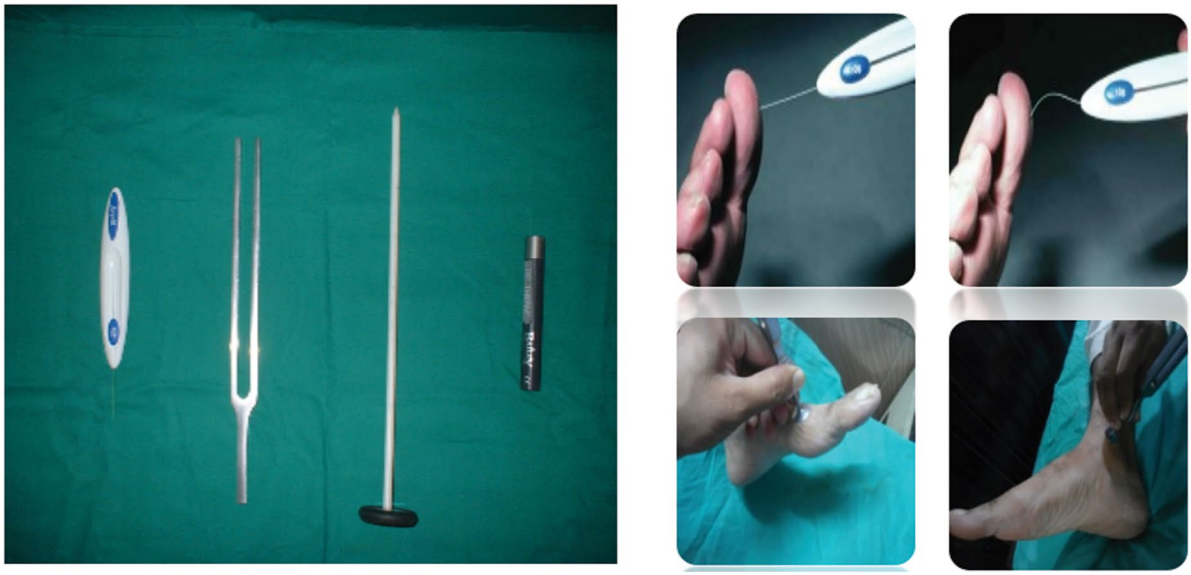

Fig.2: Examples of ischemic ulcers

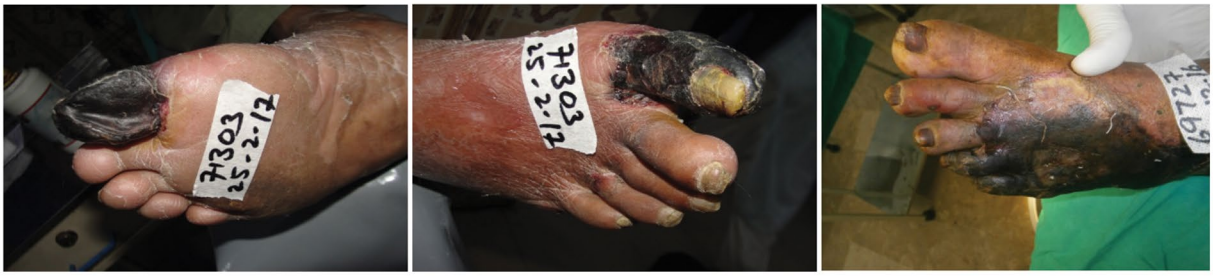

Fig.3: Examples of neuropathic ulcers

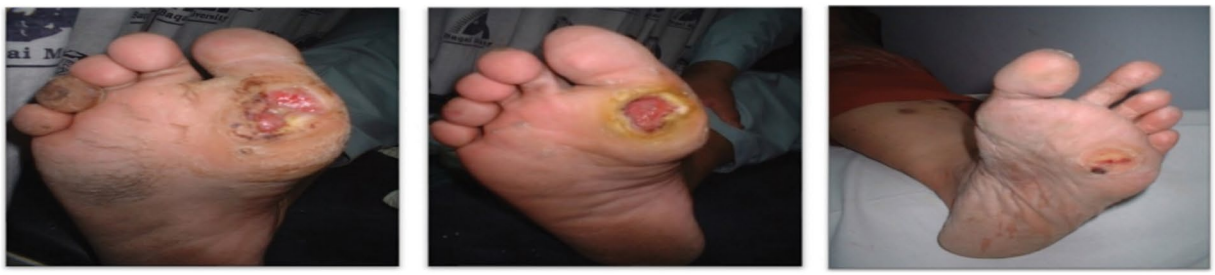

Fig.4: Custom made shoes for foot ulcers prepared with local economical material

9.3 Warning signs of foot problems[4]

- Burning or tingling in the feet or painful feet
- Loss of sensation of heat, cold, or touch
- Changes in color or shape of feet
- Loss of hair on the toes, feet, and lower legs
- Thickening and color change of the toenails
- Onset of blisters, sores, ulcers, infected corns, or ingrown toenails

9.4 Daily Foot Care

- Adopting legs crossing position while sitting or standing in one position for long periods of time should be discouraged.
- Feet and toes should be inspected daily looking at the top and the sides of feet, the soles, the heels, and the area in between the toes. Doctor should be consulted immediately if sores, redness, cuts, blisters, or bruises are observed.
- Wash feet every day in tepid water with mild soap without soaking. Dry thoroughly and pat dry gently. Infections tend to develop in moist areas, so make sure to dry well the area between the toes.
- Use any available lotion or oil for dry or rough skin. Do not use lotion between toes.
- Trim toenails after washing the feet, when nails are soft. Cut straight across rather than in a curved fashion to help prevent ingrown toenails. Don't cut into the corners. Use an emery board to smooth the edges. Be careful not to cut toenails too short. Toenails can be trimmed by a podiatrist or other health care provider if eye sight of the patient is weak or if nails are thick or yellowed due to fungal infection.
- Choose comfortable, well-fitting shoes with plenty of room, especially in the toe box. Never buy tight shoes hoping they will stretch. Do not wear shoes made out of plastic or other materials that do not breathe. Choose leather, canvas, or suede. Avoid pointed-toe and high heels. Wear shoes that can be adjusted with laces, buckles, or Velcro. Inspect the inside of shoes every day, looking for tears or bumps that may cause pressure or irritation. If neuropathy is present, take off shoes after every five hours to change the pressure points on different areas of feet.
- Wear cotton socks without any pressure areas.

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CHAPTER 10

DIABETES & OBESITY

10.1 DIABETES AND OBESITY

Although, simultaneous occurrence of obesity and diabetes is not universal, excess weight is an established risk factor for type 2 diabetes.[1,2] Obesity is considered to promote type 2 diabetes through pro inflammatory cytokines, insulin resistance, deranged fatty acid metabolism, and cellular processes such as mitochondrial dysfunction and endoplasmic reticulum stress.[3] There is substantial evidence that even modest weight reduction either through lifestyle/behavioral interventions, weight reducing medicines, or bariatric surgery-can improves glycemic control and reduce diabetes risk. For those who are obese and do not have diabetes, a loss of 5% of body weight along with regular exercise can reduce risk of developing diabetes by over 50%.[4]

Determining Ideal Body Weight (lbs) Based On Height To Weight: The Hamwi Method.[1]

Frame Size	*Females*	*Males*
Medium	Allow 100 lb for first 5 ft of height plus 5 lb for each additional inch. Subtract 2.5 lb for each inch less than 5 ft.	Allow 106 lb for first 5 ft of height plus 6 lb for each additional inch. Subtract 2.5 lb for each inch under 5 ft
Small		
Large	Subtract 10%	Subtract 10%
1 lbs = 0.453 kg	Add 10%	Add 10%

10.2 Strategies for reducing body weight:

Creating a negative energy balance, i.e. consuming lower amount of calories than spent is the only method for reducing body weight. Substantial and consistent negative energy balance induces lipolysis and weight loss. This could be achieved by decreasing energy intake and/or increasing energy expenditure. Energy intake could be decreased by modifying the amount, frequency and type of food consumed.
Energy expenditure could be increased by increasing voluntary physical activity and/or increasing basal metabolic rate.

Strategies that help in achieving negative energy balance include:

1. **Lifestyle changes:**
    i) Diet: lower consumption of energy
    ii) Physical Activity higher expenditure of energy
2. **Medications**
3. **Bariatric Surgery**

DIET

Energy intake is reduced by decreasing the intake of fats and/or carbohydrates. As long as diet is providing essential fats (11-16 g linoleic acid and 1.1-1.6 g alpha linolenic acid),[5] and fulfilling minimum daily requirement of carbohydrates (130 gm) the two nutrients could be reduced in any proportion that suits the individual preferences and other health conditions. Regardless of the method chosen for inducing negative energy balance, assurance of nutritionally adequate diet is essential to prevent malnutrition and assure sustainability. Diet must provide at least 0.8-1

gm/kg protein,[6] and vitamins and minerals to fulfill age/gender specific daily requirements.[7] Negative energy balance, and weight loss, accompanied by insufficient intake of nutrients would lead to muscle loss, nutritional deficiencies and non-compliance. High carbohydrate diets make it difficult to attain or maintain energy deficit. Carbohydrate intake leads to higher amount of insulin secretion from pancreas. Insulin promotes positive energy balance as it promotes fat synthesis (lipogenesis) and storage, and inhibits fat breakdown (lipolysis). Foods that cause a rise in blood glucose, such as sugars, starches, or amino acids will stimulate the secretion of insulin from the pancreas. A diet that lowers the amount of insulin secreted is beneficial for weight loss.

General recommendations that could be given to decrease energy intake and assure diet quality include:

- Avoiding food having high proportion of starches, sugars or fat e.g. white flour chapatti, bread, rice, baked products, fried products, high-fat curries, ice creams, sweet drinks and sweets.
- Limiting intake of very sweet and starchy fruits and vegetables.
- Increasing intake of salad vegetables, water and high fiber foods.

Physical Activity

Regular activity is a key part of managing diabetes. In addition to increasing energy expenditure, it increases insulin sensitivity. Identifying factors that could motivate physical activity and exploring opportunities that can facilitate physical activity are the keys to unsustainable physical activity program. For otherwise healthy people, recommending 30 minutes of brisk walking on most days of the week is appropriate.[8] However in people having restrictive health conditions or cultural limitations, suggesting other activities that are feasible and enjoyable for them has greater chances of long term compliance. Use of pedometers and heart rate monitors where feasible can help in observing compliance and safety of exercise program.

MEDICATIONS

Currently available drugs include Phentermine (since 1959) and Orlistat(since 1999).[9]

BARIATRIC SURGERY

Bariatric surgical procedures cause weight loss by restricting the amount of food the stomach can hold, causing malabsorption of nutrients, or by a combination of both gastric restriction and malabsorption. Bariatric procedures also often cause hormonal changes. Most weight loss surgeries today are performed using minimally invasive techniques (laparoscopic surgery). The most common bariatric surgery procedures are gastric bypass, sleeve gastrectomy, adjustable gastric band, and biliopancreatic diversion with duodenal switch. Each surgery has its own advantages and disadvantages.[10]

Health benefits of bariatric surgery, determined largely from nonrandomized studies, are being increasingly recognized and include resolution of comorbidities such as diabetes, hypertension, and dyslipidemia. For extreme obesity, surgery is now the preferred and currently only effective treatment modality. Acute morbidity and mortality of surgical approaches have been dramatically reduced enabling widespread use of these procedures.[10]

Indications for bariatric surgery include morbid obesity (BMI >40) or severe obesity (BMI>35) with co-morbidities. Bariatric surgery is advisable in those patients who had made reasonable attempts to reduce body weight and demonstrate a commitment to follow post-operative recommendations, maintain necessary lifestyle changes and agree to lifelong post-operative medical surveillance.[10]

Weight (kg)	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125
Height (cm)		Underweight				Healthy Weight				Overweight				Obese			
140	23	26	28	31	33	36	38	41	43	46	48	51	54	56	59	61	64
145	21	24	26	29	31	33	36	38	40	43	45	48	50	52	55	57	59
150	20	22	24	27	29	31	33	36	38	40	42	44	47	49	51	53	56
155	19	21	23	25	27	29	31	33	35	37	40	42	44	46	48	50	52
160	18	20	21	23	25	27	29	31	33	35	37	39	41	43	45	47	49
165	17	18	20	22	24	26	28	29	31	33	35	37	39	40	42	44	46
170	16	17	19	21	22	24	26	28	29	31	33	35	36	38	40	42	43
175	15	16	18	20	21	23	24	26	28	29	31	33	34	36	38	39	41
180	14	15	17	19	20	22	23	25	26	28	29	31	32	34	35	37	39
185	13	15	16	18	19	20	22	23	25	26	28	29	31	32	34	35	37
190	12	14	15	17	18	19	21	22	24	25	26	28	29	30	32	33	35
195	12	13	14	16	17	18	20	21	22	24	25	26	28	29	30	32	33
200	11	13	14	15	16	18	19	20	21	23	24	25	26	28	29	30	31
205	11	12	13	14	15	17	18	19	20	21	23	24	25	26	27	29	30
210	10	11	12	14	15	16	17	18	19	20	22	23	24	25	26	27	28
215	10	11	12	13	14	15	16	17	18	19	21	22	23	24	25	26	27

The BMI cut-offs used in the above chart are from the following source:
BMI Calculator, Asian American Diabetes Initiative
Web site. http://aadi.joslin.org/content/bmi-calculator.

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PROMPT

Pakistan's Recommendations for Optimal Management of diabetes from Primary to Tertiary car level