महानिदेशक सशस्त्र सेना चिकित्सा सेवा चिकित्सा ज्ञापन क्रमांक 179 DGAFMS MEDICAL MEMORANDUM NO. 179

# डायबिटीज मैलिट्स DIABETES MELLITUS

(यह ज्ञापन महानिदेशक संशस्त्र सेना चिकित्सा सेवा चिकित्सा ज्ञापन क्रमांक 160 को स्थगित करता है)

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#### वितरण :---

- (क) एक प्रति प्रत्येक चिकित्सा अधिकारी को।
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## **DGAFMS MEDICAL MEMORANDUM NO. 179**

#### **Diabetes Mellitus**

#### **Definition**

1. Diabetes Mellitus can be regarded as a syndrome resulting from many causes and characterized by chronic hyperglycemia due to the deficient action of insulin on target tissues (due to inadequate insulin secretion, insulin resistance or both). The deficient action of insulin is associated with disturbances of carbohydrate, fat, protein and electrolyte metabolism. Diabetes mellitus may present with characteristic symptoms such as increased thirst, polyuria, loss of weight and blurring of vision. Quite often the individual is asymptomatic. Untreated it can lead to acute and chronic complications. Long-term complications as a result of microangiopathy include retinopathy, nephropathy and neuropathy. In addition, Diabetes patients are at increased risk of developing macrovascular diseases like coronary artery disease, cerebrovascular accidents, and peripheral vascular disease.

#### Classification of Diabetes Mellitus

- 2. Diabetes Mellitus is classified on the basis of etiology rather than age of onset or type of therapy.
  - (a) Type 1 Diabetes Mellitus, results from beta cell destruction leading to insulin deficiency and was earlier known as IDDM. It is characterized by the presence of various autoantibodies, which identify the autoimmune processes that lead to beta cell destruction. In type 1 idiopathic type, no immune markers are demonstrable.

Sometimes young lean adults present with osmotic symptoms, high blood glucose, without family history of diabetes and glutamic acid decarboxylase (GAD) antibodies. These patients initially require insulin therapy, but later may be controlled on oral drugs for short duration. Ultimately they require early insulin therapy. These subjects are labeled as Latent Autoimmune Diabetes of Adult (LADA).

(b) <u>Type 2 Diabetes Mellitus</u>, earlier known as NIDDM is the most common form of diabetes and is characterised by insulin resistance, impaired insulin secretion or both.

#### (c) Other specific types

- (i) Genetic defects of beta cell function.
- (ii) Genetic defects in insulin action.
- (iii) Disorders ofendocrine pancreas.
- (iv) Endocrinopathies.
- (v) Drug or chemical induced diabetes.
- (vi) Infections.
- (vii) Uncommon forms of immune mediated diabetes.
- (viii) Other genetic syndromes sometimes associated with diabetes.
- (d) Gestational Diabetes Mellitus (GDM)

#### Diagnostic Criteria

- 3. Following diagnostic Criteria will be adopted:-
  - (a) The diagnosis of diabetes should always be confirmed by repeating the test on another day unless there is unequivocal hyperglycemia with acute metabolic decompensation or obvious symptoms. The diagnosis of diabetes can be made by casual venous plasma glucose level of  $\geq 200 \, \text{mg/dl}$  or fasting Plasma glucose values  $\geq 126 \, \text{mg/dl}$ .
  - (b) Oral glucose tolerance test (OGTT) will not be done as part of routine screening for diabetes mellitus. If fasting and post prandial venous glucose values are equivocal, an OGTT should be performed. Value of Fasting venous Plasma Glucose ≥126 mg/dl or 2 hours Post Glucose load (PG) ≥200 mg/dl (Or bothFBG & PG) will be diagnostic of diabetes mellitus. Only fasting and 2 h post glucose values are to be taken into consideration during interpretation of results. A1C (to be performed HPLC method which is standardized to the Diabetes Control and Complications Trial (DCCT) assay) >6.5% is also indicative of diabetes mellitus.
  - (c) Pre diabetes category will consist of either Impaired Fasting Glucose (Fasting plasma glucose >100 mg/d1 but <126 mg/dl or Impaired Glucose Tolerance (Two hour post glucose load value of plasma glucose >140 but <200 mg/dl).

## Screening and Diagnosis-Gestational Diabetes Mellitus (GDM)

- 4. (a) Gestational diabetes is carbohydrate intolerance resulting in hyperglycemia of variable severity first recognised during pregnancy. Formal systematic screening for gestational diabetes is done between 24 and 28 weeks of gestation for all and during first trimester for women at high risk i.e. older age, those with previous history of GDM/glucose intolerance and macrosomia, obesity and any pregnant woman who has elevated fasting or casual venous glucose levels.
  - (b) Standard OGTTwith 75 g of glucose should be performed after overnight fasting. Plasma glucose is measured fasting and 2 hours after glucose load. GDM is diagnosed when any one of the value is abnormal among fasting  $\geq 92$  mg/dl, One hour  $\geq 180$ mg/dl, Two hour  $\geq 153$  mg/dl.
  - (c) Six weeks after delivery, a repeat OGTT with 75 g of glucose is to be carried out.
  - (d) Only insulin is recommended for the management of GDM cases to achieve desired glycemic control. There are recent reports of successful use of metformin and glibenclamide in GDM; however, these drugs are not part of current recommendations for the management of diabetes.

## Examination

- 5. All cases will be clinically assessed with special attention to following points which will be recorded in case sheets/specialist opinion for medcat:—
  - (a) Weight (Kg)
  - (b) Height (Cm)
  - (c) Body Mass Index (BMI)- calculated by weight divided by square of height
  - (d) Waist circumference/Hip circumference ratio
  - (e) Peripheral pulsations
  - (f) BP, lying and standing
  - (g) Visual acuity and fundoscopy

- (h) Signs of peripheral neuropathy
  - (i) Sense of vibration
  - (ii) Sense of position
  - (iii) Sense of touch, pain and temperature
  - (iv) Paresthesia
- (i) Skin lesions, particularly infection
- (j) Obstetrical complication (Where applicable)

A record of various complications and their severity will be made.

## **Laboratory Investigation**

- 6. (a) Following investigations will be done in all cases at the time of assessment
  - (i) Hemoglobin and blood counts
  - (ii) Urine for sugar, ketone bodies, quantitative estimation of protein (including urine for microalbuminuria where facilities exist) and microscopic examination for deposits
  - (iii) Fasting and 2 hours post prandial blood glucose. Blood glucose profile including pre and post meal (when indicated)
  - (iv) Glycosylated Hb (HbAlc) where facility exists
  - (v) Blood cholesterol (Lipid profile should be done where facility exists)
  - (vi) Blood Urea
  - (vii) Serum Creatinine
  - (b) Plasma glucose estimation will be done by glucose oxidase/peroxidase or hexokinase method. To minimize glycolysis, one should place the sample tube immediately in ice-water slurry, and plasma should be separated from the cells within 30 min. If that cannot be achieved, a tube containing a rapidly effective glycolysis inhibitor, such as citrate buffer, should be used for collecting the sample. Tubes with only enolase inhibitors, such as sodium fluoride, should not be relied on to prevent glycolysis. Only venous plasma should be used for initial diagnosis or when

upgradation of medical category is considered. Capillary blood, glucose measured by glucometer should not be used for diagnosis. For routine follow-up, capillary blood may be used but sample may be unreliable if the flow of blood is not free and finger is squeezed. The nature of blood sample used for investigation should always be specified. Venous plasma glucose is 10-15% higher than venous whole blood glucose.

- (c) OGTT: The Individual should be on a normal unrestricted diet containing more than 150g of carbohydrate per day and usual physical activity for at least 72 hours before OGTT. He will not be on any hypoglycemic drugs when OGTT is done. The test should be performed in the morning after overnight fasting for 8 to 14 hours, although water may be permitted. 75g glucose in 250-350 ml water is given over 5 minutes. Glucose load for children will be 1.75g/kg up to a total of 75g of glucose. Smoking or exercise is not permitted during the test. Blood sample should be collected at fasting state and 2 hours after the glucose load.
- (d) Resting ECG:-Effort Tolerance Test by tread milltest (TMT), where considered necessary.
- (e) Imaging:-Radiograph of chest, abdomen ultrasonogram of abdomen for pancreatic calcification, renal size and echo texture will be done in all casesat initial diagnosis and subsequently during review if indicated and CT scan of abdomen in selected cases, if indications exist.

### Management

- 7. Good glycaemic control should be the aim in all cases of diabetes so as to ameliorate the symptoms and prevent the acute and long term complications. Each patient requires individual attention and care. However, general aspects of management are as follows:-
  - (a) Diet-Some form of dietary advice is needed for all diabetics. It must be simple and realistic. Rapidly absorbed sugars and refined carbohydrates must be avoided in all cases. A diet chart is to be constructed in all cases based on eating habits, weight and physical activity of the individual.
    - (i) In Type 2 diabetes mellitus, dietary management may be the only treatment required in very few cases. In obese/

overweight patients, reduction and maintenance of weight by low calorie, low fat, high fiber and adequate protein diet is advised along with regular graded exercise.

- (ii) Type I diabetes mellitus requires a less flexible diet at regular and fixed times which should adapt to the type of insulin used. However, with present basal-bolus regime they may have flexible schedule of diet. Patients on insulin pump therapy may have more flexibility in their diet.
- (b) <u>Exercise</u>—Exercise improves glucose metabolism by its utilisation by muscles. Graded regular exercise of at least 30 minutes daily suited to age and physical status must been couraged.

## (c) <u>Drugs</u>:—

- (i) Diabetic patients who are not controlled with diet and exercise, will require drugs to control hyperglycemia. Attempt should be made to control hyperglycaemia initially with oral antihyperglycemic drugs (OADs) unless the patient is ketotic and/or suffering from complications necessitating immediate control with insulin. It will be ensured that insulin is not withheld from a patient requiring it at any time.
- (ii) All attempts should be made to control hyperglycemia with OADs. Table-1 gives currently available and used OADs. Metformin to be started initially in all patients diagnosed as type-2 diabetes mellitus. Those not controlled with metformin should be given additional therapy as per Figure-1. When blood glucose levels are not normalized after a thorough trial with maximal doses of OADs even in combination, the patient should be treated with insulin. Presently available insulins are given in Table-2. The disposal of cases depends upon the mode of therapy required to achieve good glycemic control.
- (iii) Other drugs—Alpha-glucosidase inhibitors are useful for patients with post prandial hyperglycemia. Glucagon-like-Peptide-1 mimetics (Exanatide, Liraglutide) are available for the treatment of Type-2 diabetes mellitus. These drugs are given parenterally and have weight reducing properties. Amylin agonist (Pramlintide) is also parenterally administered drugs.

- (d) <u>Education and self-care</u>—The importance of selfcare should be stressed. It depends upon health education of the patient. Health education should include the following:-
  - (i) A basic knowledge of diabetes and its complications.
  - (ii) Recognition of symptoms and signs of hypoglycaemia and measures to prevent and correct it.
  - (iii) Guidelines on insulin types, storage, filling and injection technique, injection sites, proper gap between meals, and sick day guidelines for those on insulin therapy.
  - (iv) Recognition of importance of diet and regular exercise as an integral part of management.
  - (v) Maintenance of diabetic card on the person of patient at all times.
  - (vi) Care of feet, finger and toe nails, especially in those with diabetic neuropathy and vascular disease.

Table-1
Oral antihyperglycemic drugs

Name	Dose and effect	Instruction	Side effects
Metformin	1.5-2.5 gm Reduces FBG by 60-80	To be taken with meal	GIT Intolerance Contraindicated in patients with renal
Sulphonulurea	mg/dl Reduces A1C by 1.5% Reduces FBG by 60–80 mg/dl Reduces A1C by 1.5%	To be taken 30 minute before meal	and liver failure Hypoglycemia Weight gain Hypersensitivity
Glibenclamide Glynase Glicalzide	a DD		reaction
Glimeperide Glinides	Reduces FBG by 60–80 mg/dl Reduces A1C by 1.5%	To be taken before meal	As above
Repaglinide Nateglinide Pioglitazone	0.5-2 mg with each meal 60-120 mg with each meal 15-45 mg Dose OD Reduces FBG by 40-60 mg/dl Reduces A1C by 1.0%		Weight gain Edema, Bone loss Contraindicated in liver and cardiac failure

Name	Dose and effect	Instruction	Side effects
Alpha- glucosidase inhibitors Acarbose Voglibose DPP-4 inhibitors	Reduces FBG by 20–40 mg/dl Reduces A1C by 0.5% 25–100 mg Dose TDS 0.2–0.3 mg Dose TDS Reduces FBG by 40–60 mg/dl Reduces A1C by 0.9% 100 mg OD		
Vildaglitin Saxaglitin	50 mg BD 5 mg OD		

Figure-1 Diagnosis - Type-2 Diabetes Mellitus Life style modification + Metformin A1C <7% → Yes (Continue) No Add Basal Insulin Add Glitazones Add Sulphonylurea Expensive No Hypoglycemia Least Expensive Most effective Side effects Hypoglycemia Intensify Insulin Add Suphonylurea/ Add Glitazone/ Therapy DPP-4 inhibitors/ DPP-4 inhibitors/ Basal Insulin Basal Insulin Intensify Insulin Therapy

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Table-2
Insulin Preparations

Generic Name	Onset of action	Duration of action	Instructions
Regular insulin	30-60 minutes	6 Hours	To be taken 30 minutes before meal
Rapid acting Insulins (Lispro, Aspart, Gluisiline)	5-15 minutes	3-4 hours	To be taken immediately before meal
Intermediate acting insulin(NPH)	1.5–3 hours	10-12 hours	
Long Acting (Basal) insulin (Glargine, Detemir)	2-4 hours Peakless insulin	~ 24 hours	Usually given at bedtime and unrelated to meal

(e) Comprehensive Care: All diabetics should be advised to maintain following targets as a part of comprehensive care to decrease risk of cardiovascular disease:—

(i)	Fasting blood glucose	— 70–130mg/dl	
(ii)	Post prandial glucose	<180mg/d1	

(iii) HbA1c — <7.0%

(iv) Blood Pressure — <130/80 mmHg

(v) LDL Cholesterol — <100 mg/dl

These targets should be individualised according to age, duration of diabetes, associated comorbities, and longevity. All should be advised to maintain ideal body weight, to stop smoking, and given aspirin (75-150mg) to those above 50 year of age.

## **Grades of Control**

8. For assessment of "Grades of Control", the patient will be admitted in hospital and given appropriate diet depending on his/her requirements. Drugs will be continued in the usual schedule. A

detailed clinical examination will be carried out to detect any complication of diabetes. OGTT is not required to judge the grade of control of diabetes mellitus.

- (a) Grade III control: When targets are achieved as per para 7(e).
- (b) Grade II control: When targets are maintained for 6 months and complications of diabetes, if present earlier, have stabilized or completely regressed.
- (c) Grade I control: When grade Il control is maintained for at least 12 months and there are no complications, or complications, if present earlier, have completely regressed.

#### Disposal

- Disposal regarding retention or categorisation of all ranks for diabetes will be given within three months of diagnosis and starting treatment. It may be extended to six months in patients requiring insulin.
  - (a) All ranks requiring long term insulin treatment will be placed initially in medical classification P3 (T24) and subsequently in lower medical classification P3 (permanent), if on insulin. They will be retained in service if glycemic control is achieved on OADs with single dose of long acting Insulin (≤40IU per day). The individuals on Insulin will be recommended not to be posted to places with extreme climates (making storage of insulin difficult) and to be posted to places with basic medical facilities (with MO/RMO in station).
  - (b) All ranks controlled on diet/oral drugs:
    - (i) Those who do not achieve Grade III control may be placed in medical cat P3 (T-24) and subsequently P3 (Perm).
    - (ii) Those who achieve grade II control will be upgraded to med cat P2 (T-24) and subsequently P2 (Perm).
    - (iii) When Grade II control has been achieved and maintained for at least one year and there are no

complications, or complications, if present earlier, have completely regressed (i.e. Grade I control has been achieved), with diet and exercise only (no drugs), and the patient is not on any OADs and OGTT is normal, upgradation to medical category P-1b may be considered. Such cases should be screened for microalbumunuria and A1C levels, which should be in normal range. Opinion of Endocrinologist/Senior Adviser (Medicine & Endocrinology) as concurred by Consultant/Senior Consultant (Medicine) will be required for upgradation. Such personnel will be reviewed by a medical specialist during annual medical examination for a period of at least 3 years and an entry of 'Diabetes Mellitus Remitted' will be made in the health record card medical documents.

- (c) Opinion of Endocrinologist/Senior Adviser (Medicine & Endocrinology) should be obtained before patient is considered for invalidment. Following patients will be invalided out of service:—
  - (i) If PBORs require insulin dose (>40IU/day) or multiple subcutaneous insulin therapy for glycemic control.
  - (ii) Patients who develop unstable serious complications like recurrent DKA, brittle diabetes.
  - (iii) All ranks developing serious complications at any time while on follow-up.
- 10. Cases diagnosed as Prediabetes will be disposed off as under:-
  - (a) Officers will be placed in med cat P1(b) and advised life style modifications. If OGTT becomes normal, they will be upgraded to med cat P1 at the time of review. If Prediabetes persists they will be placed in med cat P2 (Permanent) at the end of one year.
  - (b) PBORs will be placed in med cat P2(T-24+24) and advised life style modifications. If at the end of one year, OGTT is normal, they will be upgraded to med cat P1. If Prediabetes persists they will be placed in med cat P2 (Permanent).