

When a patient is first seen with a random blood sugar value of 208 mg/dl several clinical issues arise and several questions need to be answered. These include :

1. Does the patient have diabetes mellitus or stress hyperglycaemia ?
2. How do we confirm the diagnosis of diabetes mellitus?
3. What is the type of diabetes mellitus?
4. Does the patient have any of the long term complications of diabetes Mellitus?
5. Does the patient have any other comorbidity?
6. What are the management Issues in this patient?
 - a. Glycaemic management – what should be the approach?
 - b. Management of complications and comorbidities - Approach ?
7. How should I monitor this patient ?

DOES THE PATIENT HAVE DIABETES MELLITUS OR STRESS HYPERGLYCAEMIA ?

Hyperglycaemia is often transient and can be secondary to minor or major stress – stress hyperglycaemia or due to other factors. Hence it is absolutely essential to rule out these cases of transient hyperglycaemia before labelling the patient as a diabetic. Many times the cause of stress is obvious such as a major infection, an acute coronary event or stroke etc. but sometimes this is not apparent and we need to confirm the transient nature of hyperglycaemia by further testing. In a case scenario like this we should ask for a repeat blood glucose and a glycated haemoglobin estimation. The best way to measure blood glucose here is by a fasting plasma glucose and a 2hour plasma glucose measured after 75 oral glucose. This will not only confirm the hyperglycaemia but also help make a reliable diagnosis of diabetes mellitus. HbA_{1c} will indicate the relatively long term nature of the hyperglycaemia that has lasted at least 3 months which would rule out any acute stress hyperglycaemia.

HOW DO WE CONFIRM THE DIAGNOSIS OF DIABETES MELLITUS?

A diagnosis of diabetes mellitus is confirmed by

measuring fasting plasma glucose and a 2 hour plasma glucose measured after 75 oral glucose.

Diabetes can be diagnosed on any of the following criteria¹:

- Fasting plasma glucose (FPG) ≥ 126 mg/dl* *or*
- Oral glucose tolerance test (OGTT) using 75 gms of anhydrous glucose with FPG ≥ 126 mg/dl and/or 2 hour plasma glucose ≥ 200 mg/dl *or*
- Glycated haemoglobin (HbA_{1c}) $\geq 6.5\%$ ** *or*
- Random plasma glucose ≥ 200 mg/dl in the presence of classical diabetes symptoms
- Asymptomatic individuals with a single abnormal test should have the test repeated to confirm the diagnosis unless the result is unequivocally abnormal.

WHAT IS THE TYPE OF DIABETES MELLITUS?

Once a diagnosis of diabetes mellitus is confirmed the next question is to determine the type of diabetes :

- Type 2 Diabetes Mellitus
- Type 1 Diabetes Mellitus
- Secondary Diabetes
- MODY

If the patient is obese (BMI $>$) or is centrally obese (Waist $>$ in males and in females), has clinical markers of insulin resistance such as acanthosis nigricans, skin tags , has a strong family history of Diabetes mellitus, and has presented with an insidious onset of hyperglycaemia or is diagnosed incidentally the patient is likely to be suffering from type 2 diabetes mellitus.

If the patient has a normal weight and waist ,has no family history of diabetes, and has presented with a recent onset of osmotic symptoms or diabetic ketoacidosis the likely diagnosis is type 1 diabetes mellitus.

If the patient has other features of other illness such as thyrotoxicosis, cushings syndrome or chronic pancreatitis or has been on any diabetogenic drug the likely diagnosis is secondary diabetes.

If the patient has a strong 3 generation history of diabetes, is nonobese, and is not ketosis prone he could be a case of MODY.

258 DOES THE PATIENT HAVE ANY OF THE LONG TERM COMPLICATIONS OF DIABETES MELLITUS?

The patient should be thoroughly examined for any evidence of neuropathy particularly for any abnormalities of ankle jerk and vibration sense and peripheral vascular disease. He should also undergo a fundus examination for evidence of diabetic retinopathy and a urine albumin/creatinine ratio for evidence of nephropathy.

DOES THE PATIENT HAVE ANY OTHER COMORBIDITY?

One should also look for associated hypertension clinically, evidence of CAD by electrocardiography and dyslipidaemia by measuring serum lipids.

WHAT ARE THE MANAGEMENT ISSUES IN THIS PATIENT?

Glycaemic management – what should be the approach?

Diet therapy¹

Recommended care

- High-carbohydrate diets with relatively large amounts of unrefined carbohydrate and fibre such as legumes, unprocessed vegetables and fruits are recommended. Brown rice is preferred to polished white rice.
- Protein intake equivalent to at least 15% of daily total calories is recommended.
- Intake of non-nutritive artificial sweeteners in moderate amounts may be considered
- Combining foods with high and low glycaemic indices, such as adding fibre-rich foods to a meal or snack, improves the glycaemic and lipaemic profiles.
- Cardio-protective diet should include:
 - More: leafy vegetables, vegetable salads, coarse grains, sprouted grams, spices and all other foods, which are rich in fibre and antioxidants.
 - Moderate amounts of: low fat milk and milk products, vegetable oils with monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), flesh foods (fish, chicken without skin, white of the egg) and artificial sweeteners.
 - Avoid: Alcohol, sugar, saturated fats and foods that are refined, processed, salt-rich, cholesterol-rich and deep-fried, polished rice, high fructose corn syrup.
 - Total dietary salt intake should be reduced (< 5 g/day) in population at high risk of hypertension.
- Provide access to a dietician (nutritionist) or other health-care professionals trained in the principles of nutrition, at or around the time of diagnosis offering an initial consultation with follow-up sessions as required, individually or in groups.
- Individualise advice on food/meals to match needs, preferences, and culture.
- Advise on reducing energy intake and control of

foods with high amounts of added sugars, fats or alcohol.

- Provide advice on the use of foods in the prevention and management of hypoglycaemia where appropriate.

Limited care

- Nutritional counselling may be provided by someone with training in nutrition therapy, but not necessarily a credentialed dietician (nutritionist)

Lifestyle Management¹

Recommended care

- Offer lifestyle advice to all people with type 2 diabetes around the time of diagnosis.
- Review and reinforce lifestyle modification yearly and at the time of any treatment change or if feasible at every visit.
- Review and provide ongoing counselling and assessment yearly as a routine, or more often as required or requested, and when changes in medication are made.
- Advise people with type 2 diabetes that lifestyle modification, by changing patterns of eating and physical activity, can be effective in controlling many of the adverse risk factors found in the condition.
- Introduce physical activity gradually, based on the individual's willingness and ability, and setting individualised and specific goals.
- A total of 60 min of physical activity is recommended every day for healthy Indians in view of the high predisposition to develop T2DM and CAD.
 - at least 30 min of moderate-intensity aerobic activity.
 - 15 min of work-related activity.
 - 15 min of muscle-strengthening exercises (at least 3 times / week).
- In the absence of contraindications, encourage resistance training three times per week.
- Provide guidance for adjusting medications (insulin) and/or adding carbohydrate for physical activity.
- Yogic practices lead to improvement in glycaemic control, reduction in BP, correction of dyslipidaemia, reduction of insulin resistance and correction of hyperinsulinemia, with elimination of stress
- Yogic practices can be combined with other forms of physical activity when it should be done for 30min every day while for those individuals not having other forms of physical activity, it is recommended

that yogic practices are carried out for 45-60 min to achieve the metabolic benefits.

Limited care

- The principles and content of lifestyle management are as for recommended care.
- Encourage increased duration and frequency of physical activity (where needed), up to 30-45 minutes on all days of the week, or an accumulation of at least 150 minutes per week of moderate-intensity aerobic activity (50-70% of maximum heart rate).

Targets for glycaemic control¹

Target values for glucose control for HbA_{1c} and capillary/plasma glucose are as follows:

- HbA_{1c} < 7%
- FPG < 115mg/dl
- PPPG < 160mg/dl

Individualizing therapy¹

ABCD (EFGH) approach for diabetes management

Choice of any anti-diabetic agent should take into account the patient's general health status and associated medical disorders. This patient centric approach may be referred to as the ABCD (EFGH) approach for diabetes management. As shown in the figure, for any T₂DM patient first line of therapy should be metformin unless not tolerated or contraindicated.

Age

- eGFR adjusted doses of gliptins may be a suitable addition to metformin for elderly patients in whom one will like to avoid hypoglycemia and weight gain.
- Agents belonging to AGI could also be an important choice in elderly patient. These agents have moderate efficacy but minimal side effects.
- In elderly males, glitazones may be a safer alternative in patients with preserved cardiac function. However, postmenopausal females must be spared for its use because of high predisposition to osteoporosis.
- SUs, GLP-1RA, SGLT-2 inhibitors or glinides should emerge as last choice since there are adverse effects of these agents in this age group.

BMI

- GLP-1 RA seems to be the best add on therapy for those having high BMI. This group of medications have highest weight reducing property in addition to the excellent efficacy. SGLT-2 inhibitors also have a weight reduction property. The medicines in this group have an additional advantage of excellent tolerance and can be given orally as compared to GLP-1 RA. However their glycemic efficacy seems

to be less than that of GLP-1 RA. The experience with this group of agents is less than that with GLP-1 RA.

- AGIs and gliptins are weight neutral and so can be used as third line of agents.
- The last option for such kind of patients should be SU's, insulin or glitazones since they are having weight gain properties.

CKD

- Gliptins as add on therapy with metformin are good choices. Few of the gliptins need dose adjustment as per eGFR while vildagliptin needs dose adjustment in hepatic insufficiency. Linagliptin does not require any dose adjustment in renal disease.
- Repaglinide is another agent which may be used across all stages of renal insufficiency. Similarly glitazones may be used in CKD, however, one has to be careful about fluid retention.
- Short acting sulfonylureas glipizide and gliclazide may also be used across renal insufficiency, however hypoglycemia is a huge limiting factor. AGIs may be used in patients with mild to moderate renal disease.
- Insulin may be used in any stages of renal insufficiency and is the best agent for this purpose.

Duration of diabetes

- As results of recent trials have suggested to utilize an aggressive approach in cases where duration of diabetes is less than 5 years, SU or glinide, as an add on therapy to metformin, will be the best choices, being very potent agents. Addition of glitazones may be useful at this stage.
- GLP-1 RA may score over gliptins for this indication as they are more efficacious than gliptins. Gliptins may be an option for 2nd add on agent & SGLT-2 inhibitors may also be useful as second add on agent due to their insulin independent action
- AGIs are last choices due to their moderate efficacy.

Established CVD

- In patients with established CVD, DPP-4 inhibitors may be preferred agents after pioglitazone, SGLT-2 inhibitors and AGIs because of low risk of hypoglycaemia.
- GLP-1 analogues may be good suitable alternative for patients who are overweight or obese. AGIs may be preferred in patients with postprandial hyperglycaemia.
- Pioglitazone has also been shown in different studies to reduce CVD risk.
- Recent data from EMPA-REG study has shown that SGLT inhibitors reduce CV risk and CV mortality, and may be preferred.

- High cost will prevent the use of insulin analogues, gliptins, SGLT-2 inhibitors and GLP-1 RA in most of the patients.

Glycemic status

- Good glycemic control of patients is directly correlated with efficacy of any anti-diabetic agent.
- Insulin followed by GLP-1RA, SUs and glitazones have highest efficacy in terms of reducing HbA1c.
- Gliptins, SGLT2 inhibitors or AGIs should be considered as add on therapy if these agents are not able to achieve glycemic targets.

Hypoglycemia concern

- Hypoglycemia is the biggest hurdle that any medical fraternity is facing during treatment course of diabetes.
- In patients with history of hypoglycemia or for those at high risk of hypoglycemia, GLP-1RA or gliptins should be considered as first choice with. Other options include SGLT-2 inhibitors, glitazones, and AGIs.
- Last option for such patients should be either glinides, SUs or insulin since there are high chances of hypoglycaemia with these agents.

How to use the RSSDI Diabetic Therapeutic Wheel ?

- RSSDI therapeutic wheel is designed to be a simple user friendly approach to decide the appropriate antidiabetic agent to be used in Type 2 diabetes mellitus

- When you see a patient in your clinic
- Prescribe lifestyle intervention to all and metformin to most patients as mentioned in the inner core of the wheel (white and light blue rings)
- Then identify the 2/3 most important concerns / factors (from ABCDEFGH) that you feel should influence your choice of antidiabetic agent eg. Age / CKD / finance etc.
- Identify the best choices available to you from the outer rings of the wheel (Orange and red)
- Further fine tune your choices if more concerns exist in a given patient and reach a rational final choice in an 'individualised approach'

Management of complications and comorbidities - Approach ?

Management of all the complications as well as comorbidities is as important as managing glycaemia in diabetes and should be undertaken along established lines.

In conclusion, there are several clinical issues that need to be focussed on when a patient presents with a high random blood sugar value and the treating physician should adopt a systematic and practical approach to address these issues to provide appropriate management and care.

REFERENCES

1. Madhu SV, Saboo B, Makkar BM, Reddy GC, Jana J, Panda JK et al. RSSDI Clinical Practice Recommendations for Management of Type 2 Diabetes Mellitus. *IJDDC* 2015; 35:1-71.