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CASE LEARNING POINTS



- DEFINITION
- CLASSIFICATION
- PATHOGENESIS
- RISK FACTORS
- CLINICAL FEATURES
- DIAGNOSIS AND INVESTIGATIONS
- COMPLICATIONS
- TREATMENT
- GESTATIONAL DIABETES



Case 1



- A 42yr old newly employed office executive
- While undergoing routine office medical check up
- Found to have a fasting plasma glucose of 9.0mmol/l and
- A blood pressure of 110/80mmhg,
- No other presenting symptoms
- Otherwise, stable.





- 1. Is the patient diabetic?
 - a. Yes
 - b. No
 - c. It depends
 - d. I don't know





- 2. How will you make a diagnosis of diabetes in the patient?
 - a. Repeat Fasting Blood Sugar
 - b. Oral Glucose Tolerance Test
 - c. Glycosylated Hemoglobin
 - d. All of the above
 - e. None of the above





- 3. Is there any additional history you would want to get from the patient?
 - a. Yes.
 - b. No.
 - c. I don't know



Definition



- 1. Heterogeneous endocrine/metabolic disorder
- 2. Affecting mainly carbohydrate, fat and protein
- 3. Characterized by hyperglycemia
- 4. Due to relative or absolute insulin deficiency
- 5. Associated with long-term complications



Epidemiology



 Diabetes is found in every population in the world and in all regions, including rural parts of low- and middle-income countries

The number of people with diabetes is steadily rising, with WHO estimating there were 422 million adults with diabetes worldwide in 2014

- The age-adjusted prevalence in adults rose from 4.7% in 1980 to 8.5% in 2014
 - the greatest rise in low- and middle-income countries compared to high-income countries



Epidemiology -2



- In addition, the International Diabetes Federation (IDF) estimates that 1.1 million children and adolescents aged 14–19 years have T1DM
- Without interventions to halt the increase in diabetes, there will be at least
 629 million people living with diabetes by 2045
- High blood glucose causes almost 4 million deaths each year,
- The IDF estimates that the annual global health care spending on diabetes among adults was US\$ 850 billion in 2017



Epidemiology -3



- In 2021, according to IDF, Nigeria had a 3.7% prevalence of diabetes in the adult.
- The pooled prevalences of DM in the six geopolitical zones of Nigeria were:
 - 3.0% (95% CI 1.7–4.3) in the north-west,
 - 5.9% (95% CI 2.4–9.4) in the north-east,
 - 3.8% (95% CI 2.9–4.7) in the north-central zone,
 - 5.5% (95% CI 4.0–7.1) in the south-west,
 - 4.6% (95% CI 3.4–5.9) in the south-east, and
 - 9.8% (95% CI 7.2–12.4) in south-south zone .



Epidemiology -4



- The effects of diabetes extend beyond the individual to affect their families and whole societies.
- It has broad socio-economic consequences a
- It threatens national productivity and economies,
 - especially in low- and middle-income countries where diabetes is often accompanied by other diseases.



WHO Classification of Diabetes Mellitus cardiocare

- 1. Type 1
- 2. Type 2
- 3. Hybrid forms
- 4. Other Specific Types
- 5. Unclassified
- 6. Hyperglycemia first detected in Pregnancy

Type 1 diabetes Type 2 diabetes Hybrid forms of diabetes Slowly evolving immune-mediated diabetes of adults Ketosis prone type 2 diabetes Other specific types (see Tables) Monogenic diabetes Monogenic defects of β-cell function Monogenic defects in insulin action Diseases of the exocrine pancreas Endocrine disorders Drug- or chemical-induced Infections Uncommon specific forms of immune-mediated diabetes Other genetic syndromes sometimes associated with diabetes Unclassified diabetes This category should be used temporarily when there is not a clear diagnostic category especially close to the time of diagnosis of diabetes Hyperglyacemia first detected during pregnancy Diabetes mellitus in pregnancy Gestational diabetes mellitus

7th Abuja Cardiovascular Symposium 2023

Pathogenesis-Type 1



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HLA-associated, immune-mediated 1A)

- Concordance rate varies, up to 50%
- multiple genetic loci contributes to diabetes risk
- Both HLA DR3 and DR4- haplotypes contributes to diabetes risk (DQ2 and DQ8 strongest susceptibility)
- strongest protective haplotype is DQB1*0602

Autoimmunity:

occurs early in life e.g. anti-GAD, AIA, anti-Islet cell antibody

Environmental factors:

congenital rubella, CMV, bovine milk etc.



Pathogenesis-Type 2



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Genetic predetermination:

■ ~50% concordance rate

Environmental factors:

Early: Low birth weight

Late: Obesity, sedentary, ageing

Pre-diabetes:

• Insulin resistance and β-cells failure



Risk Factors for Type 2



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Risk factors for development of type 2 diabetes:

- Family history of diabetes (i.e., parent or sibling with type 2 diabetes)
- Obesity (BMI 25 kg/m2)
- Habitual physical inactivity
- Race/ethnicity (e.g., African American, Hispanic American, Native American, Asian American, Pacific Islander)
- Previously identified IFG or IGT
- History of GDM or delivery of baby 4 kg (9 lb)
- Hypertension (blood pressure 140/90 mmHg)
- HDL cholesterol level 35 mg/dL (0.90 mmol/L) and/or a triglyceride level 250 mg/dL (2.82 mmol/L)
- Polycystic ovary syndrome or acanthosis nigracans
- History of vascular disease



Clinical Features



- Asymptomatic
- Classical symptoms:
 - polyuria, polydipsia and weight-loss
- Type 1 Lean; Type 2 Overweight
- Short Onset: in type 1; Insidious Onset type 2
- ± features of long-term complications in type 2
- ± other autoimmune diseases in type 1



Case 2



- A 38yr old woman who presented in the ER
 - history of weight loss, polydypsia, polyuria,
 - generalized body weakness with blurring of vision and
 - painful sensations on both feet.
 - There is a positive family hx of diabetes in both parents of which the father died of diabetic complications.
- RBS on presentation was 26.9mmol/l
- Blood pressure 160/100mmHg





- Is the patient diabetic?
 - 1. Yes
 - 2. No
 - 3. It Depends
 - 4. I don't know





- What type of diabetes is she more likely to have?
 - 1. Type 1
 - Type 2
 - 3. Hybrid forms
 - 4. Unclassified
 - 5. None of the above





- What other investigations are very important in the management of this patient?
 - 1. Full Blood Count
 - 2. Abdominal CT Scan focus on the pancreas
 - 3. Liver Function Tests
 - 4. All of the above
 - 5. Many others, but None of the above





- What is your target BP?
 - 1. <150/90
 - 2. <140/90
 - 3. <130/80
 - **4**. <125/75
 - 5. It depends





- What other possible complications can she have?
 - 1. Diabetic Nephropathy
 - 2. Diabetic Neuropathy
 - 3. Diabetic Cheiroarthropathy
 - 4. Diabetic Retinopathy
 - 5. I don't know



Diagnosis and Investigations



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□Methods

- 1. Blood glucose: FPG, 2HPG, RBS
- 2. OGTT: not used routinely for diagnosis: only for borderline, IGT and Gestational DM

□ Criteria (WHO, 1999)

- 1. Symptomatic:
 - 1. Single FPG ≥126mg/dl (7mmol/L); OR

- 2. RBS/2HPG/OGTT ≥200mg/dl (11.1mmol/L)
- 2. Asymptomatic: Repeat another occasion
- ☐Others: C-peptides, auto antibodies
- IGT: FPG<7mmol/L, 2-hr postglucose 7.8-11 mmol/L
- IFG: FPG 6.1-6.9, 2-hr post-glucose<7.8



Descriptor	Definition
WHO-defined IFG	FPG 6.1–6.9 mmol/l
ADA-defined IFG	FPG 5.6–6.9 mmol/l
IGT	FPG <7.0 mmol/l and 2-h post-75-g OGTT glucose value ≥7.8 mmol/l and <11.1 mmol/l
Impaired glucose regulation	IFG as defined by WHO and/or IGT
Prediabetes (defined by the ADA)	FPG 5.6–6.9 mmol/l and/or HbA _{1c} 39–47 mmol/mol (5.7–6.4%) and/or 2-h post-75-g OGTT glucose value ≥7.8 mmol/l and <11.1 mmol/l
Non-diabetic hyperglycaemia	FPG 5.5–6.9 mmol/l and/or HbA _{1c} 42–47 mmol/mol (6.0–6.4%)

ADA, American Diabetes Association; FPG, fasting plasma glucose; IFG, Impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.





Other Investigations



- Fasting lipid profile
- ECG
- Electrolytes, urea & creatinine
- Urinalysis
- Microalbuminuria



Monitoring



- Urine testing
- Blood glucose lab or glucometer
- Glycated Hb
 - addition of glucose moiety to β-chain of Hb
 - test control in the last 2-3 months
- Glycosylated proteins: (fructosamine): test control for about 2-3 weeks



Diabetic Complications



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Can be classified broadly into two:

I. Acute/metabolic complications

II. Chronic complications



Acute Complications



- Metabolic
 - a) Diabetic ketoacidosis
 - b) Hyperosmolar hyperglycaemic state
 - c) Lactic acidosis
 - d) latrogenic hypoglycaemia
- Infections:
 - usually bacterial e.g. UTI, acute chest infections, abscess, sepsis, malignant otitis externa, mucormycosis



Chronic Complications



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Vascular: microvascular and macrovascular

Neurologic

Others: skin, eye, bones and joints, pregnancy-related



Vascular Complications



- Microvascular:
 - i) Retinopathy
 - ii) Nephropathy
 - iii) Neuropathy
- Macrovascular:
 - i) Stroke
 - ii) Peripheral vascular disease
 - iii) Coronary artery disease
 - iv) Cardiomyopathy



Neurological Complications



- Peripheral neuropathy
 - -Distal symmetric polyneuropathy
 - -Motor neuropathy (diabetic amyotrophy, foot drop, wrist drop)
- Cranial neuropathy: CN III, IV, VI and VII
- Autonomic neuropathy: postural hypotension, impotence, GI dysfunction, bladder atony, loss of sweating, resting tachycardia



Other Complications



- Skin
 - a) non-infectious: diabetic dermopathy, necrobiosis lipoidica diabeticorum
 - b) infectious e.g. candidiasis
 - c) mixed: diabetic foot syndrome
- Eye:
 - cataract, glaucoma, diabetic ophthalmoplegia
- Bones and joints:
 - Dupuytren's contracture, diabetic cheirarthropathy, Charcot's joint
- Pregnancy-related:
 - a) maternal: recurrent abortions, polyhydramnious, infertility
 - b) fetal: macrosomia, congenital malformations, hypoglycaemia



Case 3



- A 40yr old business man, who was recently diagnosed to be diabetic with
 - RBS of 19mmol/l following osmotic symptoms of polyuria and polydipsia,
 - there is associated calf pain while walking,
 - blurring of vision and burning sensations on the feet.
- On examination, nil of note
- Investigation result showed
 - Normal EUCR and urinalysis
 - Deranged Fasting Lipid Profile



Case 3; Discussion Questions



- What is the aim/principles of the management of this patient
- How do you manage such patient



Treatment



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Aims

- 1. To alleviate symptoms
- 2. Blood glucose control
- 3. Prevent, delay or minimize complications
- 4. Reduce morbidity and mortality



Comprehensive Targets



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Blood glucose:

FPG: <110mg/dl (6.0 mmol/L)</p>

■ Postprandial: <140mg/dl (7.0mmol/L)

■ HBA1c: <7%

Lipid profile:

- Triglycerides <150mg/dl
- LDL-C: <100mg/dl
- Total cholesterol: < 150mg/dl
- HDL-C: Males- >40mg/dl; Females > 50mg/dl

Blood Pressure:

- Systolic <130mmHg;</p>
- Diastolic < 80mmHg

BMI:

■ 20-25kg/m²

Waist circumference:

Males <100cm; Females < 88cm</p>



Education



- Main goal is patient empowerment:
 - Self-monitoring of blood glucose, blood pressure
 - Immediate management of hypoglycaemia
 - Foot care and foot wear
 - Cooperation with physician in meeting goals
 - Lifestyle adjustments



Lifestyle measures



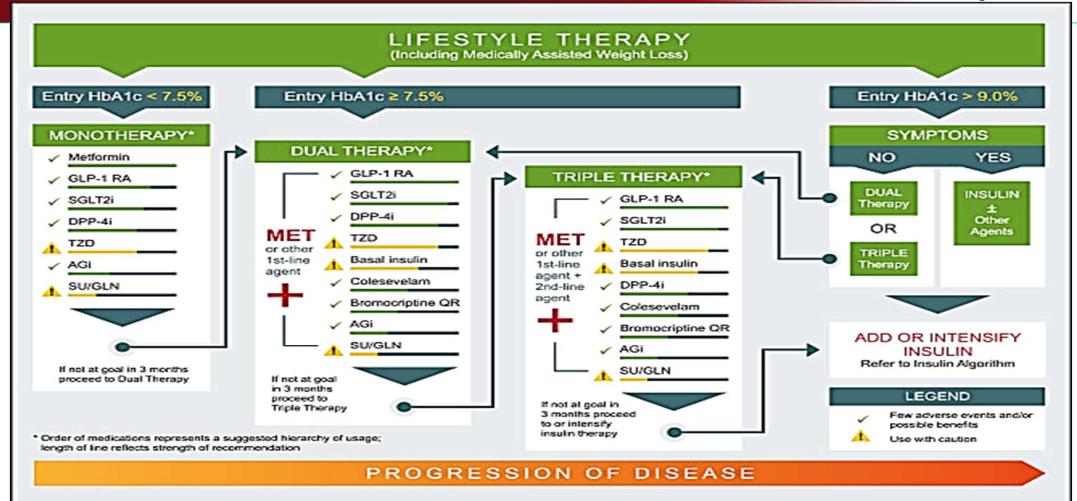
- Exercise: program planned with the Physician:
 - At least 30 minutes thrice weekly (if no C/I)
 - Avoid weight bearing or lifting. Examples of recommended exercises include brisk walking, jogging, bicycling, swimming.
- Dietary measures: individualized, on-going
 - Refined sugars: Drastic reduction
 - Complex carbohydrate: 50-60% of total calorie/day

- Fiber: Increase fiber intake
- Protein: 10-20% of total calorie/day
- Fats: Limit intake of saturated fat and dietary cholesterol; should take <30% of total calorie/day
- Salt: moderate low intake
- Alcohol: discourage in overweight/obese; generally reduce, subtract amount taken from total calorie for the day
- Weight-loss program for overweight or obese subjects



Oral hypoglycemic agents

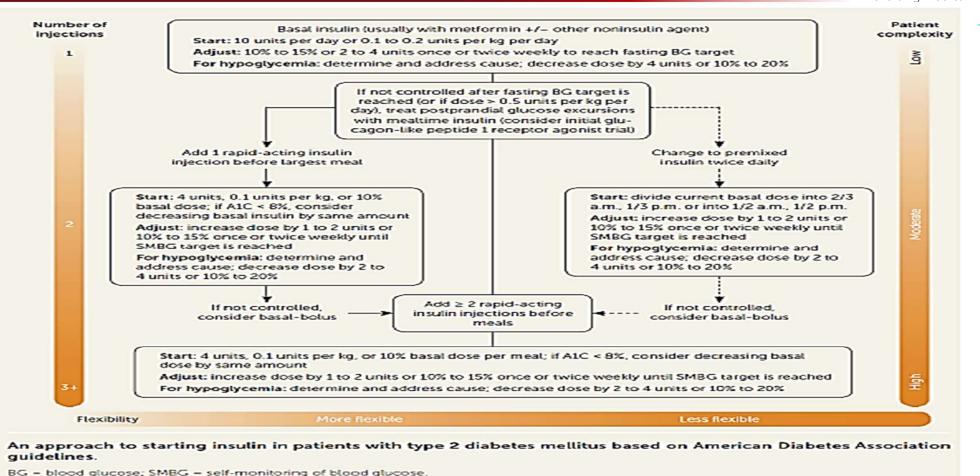




Use of Insulin in T2DM



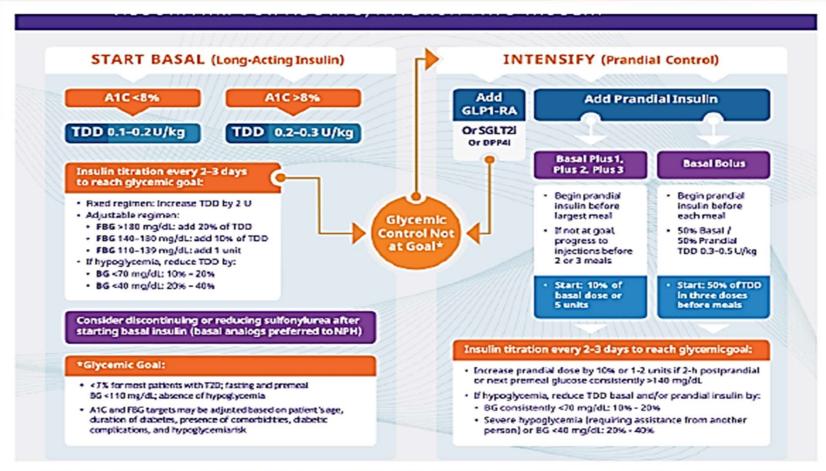
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Adapted with permission from Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes.

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Figure 3 : American Association of Clinical Endocrinologist Guidelines on Insulin Inititation

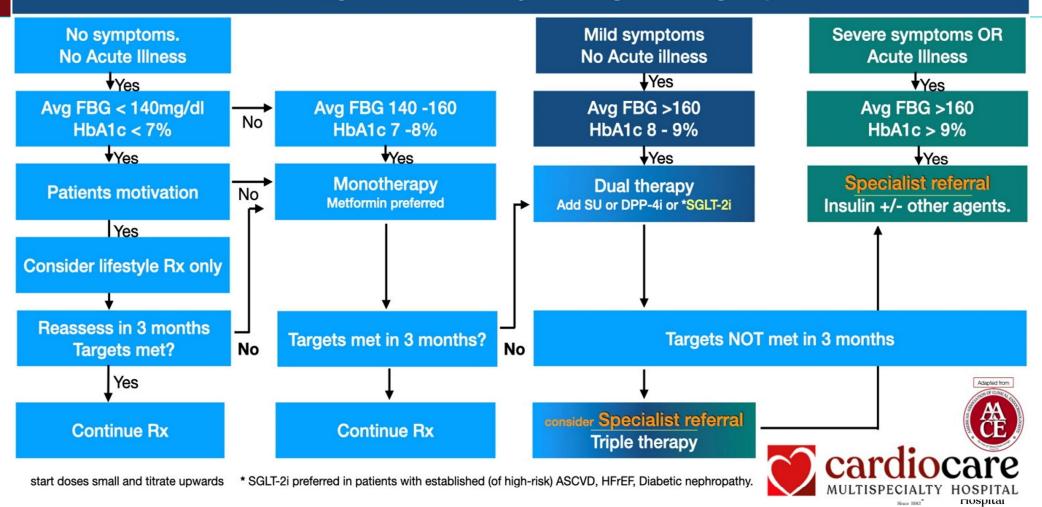




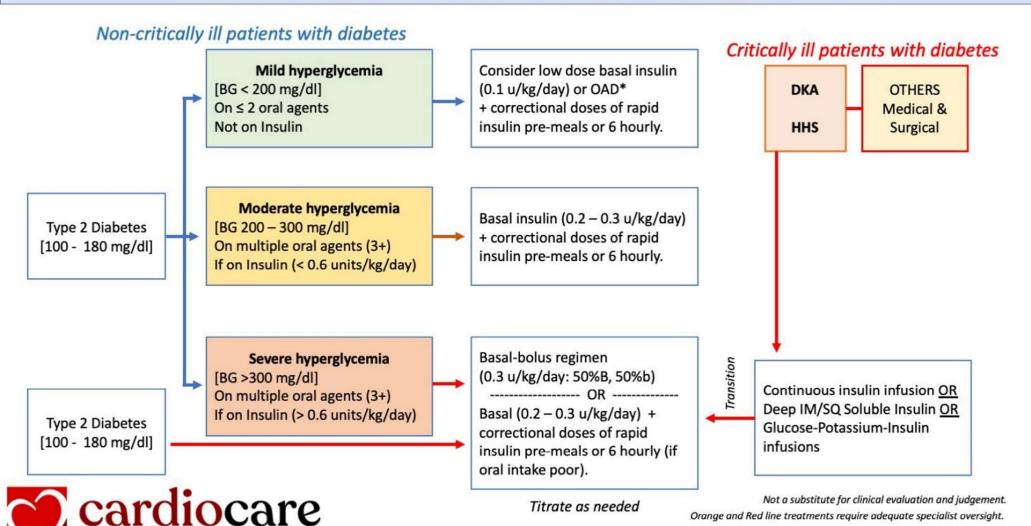
Glycemic control algorithm



Encourage diet and lifestyle changes in all groups.



Inpatient glycaemic management guidiance



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Adapted from; Francisco JP et al; Lancet Diabetes and Endocrinology; 2021

Case 4



- A 37yr old teacher, presented to the gynaecology emergency at 14weeks of gestation with a RBS of 13mmol/l.
- She has had two previous pregnancies carried to term.
 - 1. Which other history will you be interested in making a diagnosis.
 - 2. What is your diagnosis



Case 5



- A 42yr old business woman presented to the clinic at a gestational age of 27weeks with a FBS of 5.6mmol/l,
- There is a previous history of macrosomic babies in the past two pregnancies.
 - What is the diagnosis?
 - 2. What is the reason for the diagnosis





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Criteria	Diagnosis
IADPSG (75 gram OGTT) [6]	At least one value meeting the threshold: Fasting plasma glucose ≥ 5.11 mmol/l 1-h plasma glucose ≥ 10 mmol/l 2-h plasma glucose ≥ 8.5 mmol/l
Old ADA (100g OGTT) [11]	At least two values meeting the thresholds: Fasting plasma glucose ≥ 5.28 mmol/l 1-h plasma glucose ≥ 10 mmol/l 2-h plasma glucose ≥ 8.61 mmol/l 3-h plasma glucose ≥ 7.78 mmol/l
WHO (75 g OGTT) [12]	At least one value meeting the threshold: Fasting plasma glucose ≥ 7 mmol/l 2-h plasma glucose ≥ 7.78 mmol/l

IADPSG, International Association of Diabetes and Pregnancy Study Groups; ADA, American Diabetes Association; WHO, World Health Organisation.



Risk factors for GDM



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- Previous gestational diabetes.
- A large baby in their last pregnancy, e.g. >4.5kg.
- A previous unexplained stillbirth/perinatal death.
- Maternal obesity (BMI above 30kg/m2).
- Family history of diabetes (first-degree relatives).
- Family origin with a high prevalence of type 2 diabetes:

South Asian.

Black Caribbean.

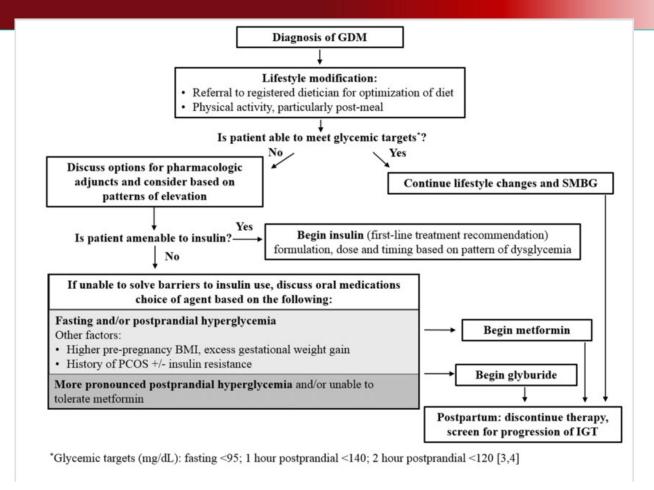
Middle Eastern.

Polyhydramnios



Management of GDM







Management of GDM



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Box 13.16 Checklist for gestational diabetes during clinic visit

- Monitoring BG, aim:
 - Fasting BG <5.9mmol/L.
 - 1h postprandial BG <7.8mmol/L (some advocate lower BG targets for obese women, e.g. <5.1 fasting and <7.0 after meals).
- · Monitor maternal weight, BP, and urinalysis.
- Monitor fetal size (abdominal circumference)—increase treatment if abdominal circumference ≥70th percentile.
- Treatment:
 - · Diet and lifestyle advice.
 - Oral hypoglycaemic agents if diet and exercise inadequate or incipient macrosomia: metformin/glibenclamide; insulin therapy— NPH and/or rapid-acting insulin analogues (aspart and lispro).
- · Reinforce dietary advice throughout pregnancy.
- Advice on physical activity (at least 30min daily).
- At 36 weeks' clinic visit, discuss and document:
 - · Mode and timing of delivery.
 - BG management and insulin infusion rate for delivery.
 - Increased risk of type 2 diabetes and evidence for delaying and prevention (diet and lifestyle or metformin).
 - Benefits of breastfeeding (mother and baby).
 - Options for safe, effective post-partum contraception.
 - Post-partum follow-up—fasting glucose or OGTT 6 weeks post-delivery.







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