Diabetes and Pregnancy

An Endocrine Society Clinical Practice Guideline

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Diabetes and Pregnancy

Overt Diabetes

• Women diabetic before the onset of pregnancy

Gestational diabetes

• Diabetes first detected in course of pregnancy
Gestational diabetes

Current definition

- Any degree of glucose intolerance with onset or first definition during pregnancy

Definition supported by ES

- The condition associated with degrees of maternal hyperglycemia less severe than those found in overt diabetes but associated with an increased risk of adverse pregnancy outcomes
Gestational diabetes - Pathophysiology

- Insulin resistance emerging in the 2nd trimester of pregnancy
  - Progesterone
  - Cortisol
  - Human placental lactogen
  - Prolactin and estrogen also contribute

- Some pts. cannot balance insulin needs and develop GDM

- Placental insulinase enzyme and obesity
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- Preconception care of women with diabetes
- Gestational diabetes
- Glucose monitoring and glycemic targets
- Nutrition therapy and weight gain targets for women with overt or gestational diabetes
- Blood glucose-lowering pharmacological therapy during pregnancy
- Labor, delivery, lactation and postpartum care
Diabetes and Pregnancy
ES Guidelines 2013
Preconception care of women with diabetes
1.1 – Preconception counselling to all diabetic women

- Sufficient glycemic control
- Assessment of comorbidities
- Discontinuing unsafe medications
- Folate supplementation
- Smoking cessation
1.1 – Preconception counselling to all diabetic women

1. Better preconception glycemic control
2. Lower rates of congenital anomalies and spontaneous abortions
1.2 – Achieve blood glucose and HbA1c close to normal

Maternal Hyperglycemia in first few wks of pregnancy

- Fetal malformations
- Spontaneous abortions
- Perinatal mortality
1.2 – Achieve blood glucose and HbA1c close to normal

Risk of congenital anomaly vs. HbA1c levels
Preconception care of women with diabetes

1.3a – Insulin therapy

- Multiple daily doses of insulin or, Continuous sc insulin infusion
- Split-dose, premixed insulin therapy

1. More likely to achieve target levels
2. Flexibility
1.3b – Insulin therapy

Change/start insulin regimen in advance

1. Better expertise of patient
2. Optimization
1.3c – Insulin therapy

- Rapid-acting insulin analog vs Regular insulin

1. Achieve postprandial B.G. targets better
2. Less risk of hypoglycemia
3. Greater lifestyle flexibility and better quality of life
4. Insulin lispro and Insulin aspart safe in pregnancy
1.3d – Insulin therapy

CONTINUE Long-acting insulin analogs

Long-acting Insulin analogs vs Intermediate acting Insulin

1. Lower rates of nocturnal hypoglycemia
2. Insulin detemir approved for use in pregnancy (Category B)
3. Insulin glargine safe in pregnancy

1. NPH is cheaper
Preconception care of women with diabetes

1.4 – Folic acid supplementation

- Start 3 months before conceiving
- 5 mg daily dose

↓ Risk of Neural tube defects
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Preconception care of women with diabetes

1.5a – Ocular care

Detailed ocular assessment

- Retinopathy present
  - Patient counselling for risk of worsening

- Retinopathy needing therapy
  - First treat retinopathy
  - Conceive only when it is stabilized
Preconception care of women with diabetes

1.5b – Ocular care

Women with Established Retinopathy

Ocular assessment every trimester

Post-pregnancy assessment within 3 months after delivery
Preconception care of women with diabetes

1.5c – Ocular care

Women with No Retinopathy

Ocular assessment soon after conception

Then, periodically as indicated
1.6 – Renal function

Renal dysfunction in Type 1 DM

↑ Risk of Adverse Maternal & Fetal outcomes (e.g. preeclampsia)

Mild Preconceptional Renal dysfunction

Reversible worsening

Mod-Severe Preconceptional Renal dysf.

Irreversible worsening
1.6a – Preconceptional Renal function assessment

1.6b – Regular renal function monitoring during pregnancy in women with preconceptional renal dysfunction
1.7a – Management of Hypertension

- Satisfactory BP Control → <130/80 mm Hg
- Preconceptional Uncontrolled HTN → ↑ Risk of Adverse outcomes (e.g. preeclampsia)
Preconception care of women with diabetes

1.7b – Management of Hypertension

ACE Inhibitors or Angiotensin-receptor blockers

Safer alternatives:
- Methyldopa
- Labetalol
- Diltiazem
- Clonidine
- Prazosin
1.7c – Management of Hypertension

Exception for using ACEI or ARBs:

- Severe renal dysfunction with uncertainty about conception

Loss of Renal protective properties vs Risk of teratogenesis

Preconception care of women with diabetes
1.7d – Management of Hypertension

If ACEI or ARBs continued up to time of conception

DISCONTINUE immediately upon confirmation of pregnancy
Preconception care of women with diabetes

1.8a – Elevated vascular risk

If vascular risk factors present

Screen for CAD before conceiving
Preconception care of women with diabetes

1.8b – Elevated vascular risk

If CAD present

✓ Severity assessment
✓ Management
✓ Counselling
Dyslipidemia seldom poses threat during pregnancy

2. Unproven safety of statins, fibrates and niacin during pregnancy
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Preconception care of women with diabetes

1.9a – DO NOT use Statins

1.9b – DO NOT use Fibrates or Niacin

1.9c – Bile acid-binding resins may be used to treat hypercholesterolemia
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Preconception care of women with diabetes

1.10 – Thyroid function assessment

- Autoimmune thyroid
- Hypothyroidism
- Type 1 DM

- Uncontrolled Hypothyroidism

- ↓ Fertility
- ↑ Risk of spontaneous abortion
- ↑ Risk of Impaired fetal brain development
1.10 – Thyroid function assessment

- Serum TSH
- Thyroid peroxidase Antibodies
1.11 – Weight reduction in overweight/obese

Severe calorie restriction (<1500 kcal/d or 50% reduction)

↑ Ketosis

Impaired fetal brain development
1.11 – Weight reduction in overweight/obese

- Severe calorie restriction (<1500 kcal/d or 50% reduction)
- Moderate calorie restriction (1600-1800 kcal/d or 33% reduction)
2.1 Universal testing for overt diabetes in non-diabetic women at first prenatal visit (<13 wks gestation)

- Fasting Plasma glucose, or
- HbA1c, or
- Untimed Random plasma glucose
2.1 Universal testing for overt diabetes in non-diabetic women at first prenatal visit

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Fasting Glucose</th>
<th>Random Glucose</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overt Diabetes</td>
<td>( \geq 126 \text{ mg/dL} )</td>
<td>( \geq 200 \text{ mg/dL} )</td>
<td>( \geq 6.5 % )</td>
</tr>
<tr>
<td>Gestational Diabetes</td>
<td>92-125 \text{ mg/dL}</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
2.1 Universal testing for overt diabetes in non-diabetic women at first prenatal visit

If Overt diabetes on screening test but no Symptoms of hyperglycemia

Second test to confirm diagnosis (Fasting glucose, Random glucose, HbA1c or OGTT)
2.2 Testing for gestational diabetes at 24 to 28 weeks gestation by using 75-g OGTT

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Fasting Glucose</th>
<th>1 hr Glucose</th>
<th>2 hr Glucose</th>
</tr>
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<tbody>
<tr>
<td>Overt Diabetes</td>
<td>≥ 126 mg/dL</td>
<td>NA</td>
<td>≥ 200 mg/dL</td>
</tr>
<tr>
<td>Gestational Diabetes</td>
<td>92-125 mg/dL</td>
<td>≥ 180 mg/dL</td>
<td>153-199 mg/dL</td>
</tr>
</tbody>
</table>
2.3 Management of elevated blood glucose

2.3a – Target blood glucose levels close to normal

2.3b - Medical Nutrition therapy +
Daily moderate exercise (≥ 30 min)

If hyperglycemia persists

2.3c - Blood glucose-lowering pharmacological therapy
2.4 Postpartum care in GDM patients

2.4a – Fasting glucose measured for 24 to 72 hrs after delivery to rule out ongoing hyperglycemia

2.4b – 2 hr, 75g OGTT at 6 to 12 wks after delivery to rule out pre-diabetes or diabetes.
2.4 Postpartum care in GDM patients

2.4c – Child’s permanent medical record should contain:

- Child’s birth weight
- Whether born to mother with GDM
2.4 Postpartum care in GDM patients

2.4d – Counselling of GDM patients:

- Lifestyle measures to ↓ risk of Type 2 DM
- Need for planning future pregnancies
- Regular diabetic screening
2.4 Postpartum care in GDM patients

2.4e – Discontinue blood glucose-lowering medication immediately after delivery

Exception: Suspected overt diabetes with accompanying hyperglycemia
3.1 Self-monitoring of blood glucose in pregnant women with overt or gestational DM

- **Fasting**
- **Post-BF**
- **Pre-Lunch**
- **Post-Lunch**
- **Pre-Dinner**
- **Post-Dinner**
- **Bedtime**

**Post-meal either 1 or 2 hrs**
### Glucose monitoring and glycemic targets

#### 3.2a-c – Glycemic targets in overt or GDM

<table>
<thead>
<tr>
<th></th>
<th>Target values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preprandial blood glucose</td>
<td>≤ 95 mg/dL</td>
</tr>
<tr>
<td>1 hr after start of a meal</td>
<td>≤ 140 mg/dL</td>
</tr>
<tr>
<td>2 hr after start of a meal</td>
<td>≤ 120 mg/dL</td>
</tr>
</tbody>
</table>

**Target preprandial blood glucose ≤ 90 mg/dL, if possible**
3.2d – Glycemic target only in overt diabetes

HbA1c ≤ 7%

Ideally HbA1c ≤ 6.5%
3.3 – Continuous glucose monitoring be used if self-monitoring is not sufficient to assess glycemic control
Nutrition therapy and weight gain targets for women with overt or gestational diabetes
4.1 Medical nutrition therapy for all pregnant women with overt or gestational DM

- Carbohydrate controlled meal
- Adequate nutrition
- Appropriate weight gain
- Normoglycemia
- Avoid ketosis
4.2a Women with overt or gestational DM to follow Institute of medicine revised guidelines (2009) for weight gain during pregnancy
### Nutrition therapy and weight gain targets

#### Institute of Medicine revised guidelines (2009)

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>Total weight gain</th>
<th>Rate of weight gain in 2(^{nd}) &amp; 3(^{rd}) Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5 kg/m(^2))</td>
<td>12.5-18 Kg</td>
<td>0.51 Kg/wk (0.44-0.58)</td>
</tr>
<tr>
<td>Normal weight (18.5-24.9 Kg/m(^2))</td>
<td>11.5-16 Kg</td>
<td>0.42 Kg/wk (0.35-0.50)</td>
</tr>
<tr>
<td>Overweight (25-29.9 Kg/m(^2))</td>
<td>7-11.5 Kg</td>
<td>0.28 Kg/wk (0.23-0.33)</td>
</tr>
<tr>
<td>Obese (≥30 Kg/m(^2))</td>
<td>5-9 Kg</td>
<td>0.22 Kg/wk (0.17-0.27)</td>
</tr>
</tbody>
</table>

Assuming 0.5-2 kg weight gain in 1\(^{st}\) trimester
4.2b Obese women with overt or GDM should reduce calorie intake

Moderate Calorie restriction
(1600-1800 kcal/d, 33% reduction)
4.3 Limit carbohydrate intake to 35-45% of total calories

✓ 3 small to moderate sized meals
✓ 2 to 4 snacks incl. evening snacks

Minimum 175g/d Carbohydrate
4.4 Same guidelines for intake of minerals and vitamins as for women without diabetes except Folic acid

- Folic acid 5mg/d beginning 3 months before conceiving
- Folic acid dose reduced to 0.4 to 1 mg/d after 12 wks gestation
- Folic acid to be continued until completion of breastfeeding
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Blood Glucose-lowering pharmacological therapy during pregnancy
5.1a Long-acting insulin analog detemir may be initiated during pregnancy if

✔ Women needs Basal insulin

✔ NPH has resulted in or may result in hypoglycemia

Continue insulin detemir, if patient successfully taking it before pregnancy
5.1b Continue insulin glargine if pt. successfully using it before pregnancy

✓ Not FDA approved, but safe in pregnancy
5.1c Rapid-acting insulin analogs lispro and aspart be used in preference of regular insulin

Rapid-acting insulin analog vs Regular insulin
5.1d Continue using continuous sc insulin infusion during pregnancy if initiated before pregnancy. Otherwise, multiple daily dose insulin preferred.

Continuous sc insulin infusion associated with:

✓ ↑ Risk of maternal ketoacidosis
✓ ↑ Risk of Neonatal Hypoglycemia
5.2 Noninsulin antihyperglycemic agents

- Glibenclamide
- Metformin
5.2a Glibenclamide

Alternative to insulin therapy in GDM if
- Insufficient glycemic control after 1-wk trial of MNT & exercise
- Patient refuse or cannot use insulin

Insulin preferred (Glibenclamide less effective) if:
- GDM diagnosed before 25 wks gestation
- Fasting plasma glucose > 110 mg/dL
5.2b Metformin

- Cross placenta freely
- Safety in pregnancy not established
- High glycemic control failure rates
- ↑ Rates of preterm birth
5.2b Metformin

Used for GDM only if

- Insufficient glycemic control after 1-wk trial of MNT & exercise
- Patient refuse or cannot use insulin or glibenclamide
- Patient not in first trimester
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Labor, delivery, lactation, and postpartum care
6.1 Blood glucose targets during labor & delivery

Blood glucose – 72 to 126 mg/dL

- Neonatal Hypoglycemia
- Fetal distress
- Birth asphyxia
- Abnormal fetal heart rate
6.2a Lactation

Breastfeed infant whenever possible

Breastfeeding reduces risk of

✓ Childhood obesity
✓ Impaired glucose tolerance and diabetes in both mother & child
✓ Helps postpartum weight loss in mother
6.2b Lactation

Continue Metformin or glibenclamide, if needed, during breastfeeding

Metformin conc. in breast milk low

Glibenclamide not detected in breast milk
6.3 Postpartum contraception

No effect of Overt or GDM on choice of contraception
6.4 Screening for postpartum thyroiditis in Type1 diabetic women

TSH at 3 and 6 months postpartum
Preconception care of women with diabetes

- Preconception care of diabetics include counselling, ocular and renal function assessment, thyroid function assessment, screening for vascular risk factors and weight reduction in obese/overweights.
- Strict blood glucose and B.P. control be achieved in advance
- Folic acid supplementation to be started 3 months before conceiving
- Discontinue/Avoid ACEI, ARBs & anti-dyslipidemics, consider alternatives
- Assess risk of worsening retinopathy and renal dysfunction
• Universal screening of all pregnant for overt diabetes at first visit

• Test for GDM at 24-28 wks gestation by 2hr 75g OGTT

• Manage hyperglycemia initially by lifestyle therapy, if it fails then pharmacological therapy used

• Discontinue B.G. lowering therapy immediately after delivery in GDM

• 2hr 75g OGTT at 6-12 wks postpartum to rule out diabetes

• Counsel GDM patients to reduce risk of T2DM in future
Glucose monitoring and glycemic targets

- Self-monitoring blood glucose levels at least 7 times a day (or continuous glucose monitoring used) in overt or GDM patients
- Achieve glycemic targets
  - Preprandial B.G. <90mg/dL,
  - 1hr Postprandial B.G. <140mg/dL,
  - 2hr Postprandial B.G. <120mg/dL
- HbA1c <7% in overt diabetics
Nutrition therapy and weight gain targets

- Medical nutrition therapy for all pregnant with overt or GDM
- Achieve weight gain targets as suggested by Institute of Medicine
- Moderate calorie intake reduction in obese and limiting CHO intake
- Folic acid to continue from 3 months before conceiving to until completion of breastfeeding
- Intake of minerals and vitamins like other non-diabetic pregnant
Blood Glucose-lowering pharmacological therapy

- Long acting Insulin analog detemir better than NPH but expensive
- Rapid-acting insulin analog (lispro & aspart) better than regular insulin
- Insulin glargine is safe to continue during pregnancy
- Multiple daily dose insulin preferred for initiation during pregnancy
- Glibenclamide good alternative to insulin in GDM
- Metformin to be used as last option in GDM, if Insulin/glibenclamide cannot be given.
• Blood glucose to be maintained between 72 to 126 mg/dL during labor & delivery

• Breastfeeding should be done by all women, even if pt. on metformin or glibenclamide

• Screen type 1 diabetics for postpartum thyroiditis
Thank you

Presentation by Dr. Jagjit Khosla