Diabetes in Pregnancy and Gestational Diabetes Mellitus (GDM)

What are the complications of diabetes in pregnancy?¹²³

- Tight glucose control is critical in the first 42 days of pregnancy (organogenesis).
- Poor glycemic control is associated with adverse pregnancy outcomes including perinatal mortality, and congenital malformations. (1st trimester concerns re: birth defects, 3rd trimester concerns re: fetal growth and development, metabolic complications).
- All pregnant women should be screened for GDM between 24-28 weeks gestation.
- Maternal: pre-eclampsia, retinopathy, nephropathy, hypertensive disorders, caesarian deliveries, increased rates of DM post partum (20% within 9 years).
- Offspring: macrosomia and associated birth trauma, NICU admissions, still births, metabolic disturbances, feeding problems, respiratory disturbances, infant/childhood obesity and glucose intolerance.

<table>
<thead>
<tr>
<th>Pregnancy Outcome</th>
<th>Pre-Existing Diabetes *</th>
<th>Gestational Diabetes *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Morbidity/Mortality</td>
<td>7.9% (2.6%)</td>
<td>3.1% (2.6%)</td>
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<tr>
<td>Pre-eclampsia</td>
<td>13.8% (4.4%)</td>
<td>6.7% (4.4%)</td>
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<tr>
<td>Caesarian Delivery</td>
<td>33.3% (11.3%)</td>
<td>17.6% (11.3%)</td>
</tr>
<tr>
<td>Infant Morbidity/Mortality</td>
<td>13.6% (3.1%)</td>
<td>3.2% (2.3%)</td>
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<tr>
<td>Macrosomia</td>
<td>35% (10.4%)</td>
<td>15.9% (10.4%)</td>
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<tr>
<td>Hypoglycemia</td>
<td>47.8% (1.6%)</td>
<td>19.1% (1.6%)</td>
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<tr>
<td>Still births</td>
<td>1.6% (0.6%)</td>
<td>0.3% (0.3%)</td>
</tr>
<tr>
<td>Admission to NICU</td>
<td>10.4% (2.1%)</td>
<td>2.4% (1.7%)</td>
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</tbody>
</table>

*Numbers in parentheses indicate rate of outcome in pregnancy without diabetes

What are the glycemic targets for diabetes in pregnancy?¹

- Pre-existing diabetes and gestational diabetes:

<table>
<thead>
<tr>
<th>Glycemic targets</th>
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<tbody>
<tr>
<td>Pre-pregnancy: A1c (%) ≤ 7.0</td>
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<tr>
<td>Once pregnant:</td>
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<tr>
<td>FBG &amp; preprandial BG (mmol/L) 3.8-5.2</td>
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<tr>
<td>1-hour postprandial BG (mmol/L) 5.5-7.7</td>
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<tr>
<td>2-hour postprandial BG (mmol/L) 5.0-6.6</td>
</tr>
<tr>
<td>A1c (%) ≤6.0 (normal)</td>
</tr>
</tbody>
</table>

What treatments are recommended for diabetes in pregnancy and gestational diabetes?¹⁴

- Optimal glycemic control prior to conception is essential with pre-existing diabetes.
- In GDM, nutrition therapy and light exercise (e.g. walk after meals) are initial treatment. If glycemic targets are not met within 2 weeks, initiate insulin.
- Use intensive insulin therapy – multiple daily insulin injections (MDI) or continuous subcutaneous insulin infusions. No particular insulin regimen has been shown to be more effective in pregnant women requiring insulin therapy.
- Self-monitoring of blood glucose: preprandial & postprandial at least 4 times per day, with occasional nighttime monitoring.
- Care should be taken to avoid hypoglycemia as a result of striving to achieve glycemic targets. Risk of hypoglycemia is increased in Type 1 DM during the first trimester.

Which insulins are safe to use in pregnancy?¹⁴⁵⁶⁷⁸

- Regular human and NPH insulin are the most studied and have the most safety experience. A number of clinical trials evaluating some of the new insulins have been published. Lispro or Aspart have less experience, but appear to be as safe as regular human insulin. They may be preferred by patients needing the convenience of mealtime dosing.
- Women on long-acting insulin analogues, i.e. glargine or detemir, may be switched to NPH preferably prior to conception.
- There is insufficient evidence to routinely recommend glargine or detemir in pregnancy, but may be an option in women who cannot tolerate NPH because of nocturnal hypoglycemia. Theoretical risks would suggest that patients should avoid glargine use in pregnancy; however, a meta-analysis comparing glargine (n=331) to NPH (n=371) use during pregnancy found no statistically significant differences in adverse fetal outcomes.¹⁷

Can oral hypoglycemic agents be used in pregnancy?¹⁴⁸⁹¹⁰¹¹¹²¹³¹⁴¹⁵

- Historically, oral agents for diabetes were not recommended during pregnancy. Patients should generally be switched to insulin therapy and titrated to achieve acceptable glucose control before conception. However, metformin and glyburide may be continued in T2DM, or initiated in GDM females who are non-adherent to or refuse insulin. Glyburide does not cross the placenta, and neither agent appears to be teratogenic nor is excreted into breast milk. Metformin and glyburide are similar to insulin in terms of maternal and fetal outcomes. Insulin may be added to metformin if needed to achieve targets.
- Update Jan 2010: small Latina study suggests glyburide more likely to produce glycemic control than metformin.¹²
What are other important considerations in the management of diabetes in pregnancy?1,8,16

Pre-conception & Early Pregnancy
- Folic acid 5mg/d supplementation is recommended 3 months pre-conception to prevent neural tube defects and for the first 12 weeks post conception. Thereafter, supplement with 0.4-1 mg/day.
- Statins should be discontinued prior to conception due to the risk of teratogenicity.
- New evidence suggests that ACE inhibitors and ARBs during the 1st trimester may not increase the risk of fetal toxicity more than other antihypertensives. Hypertension itself may contribute to fetal toxicity.18 These medications are still contraindicated during 2nd and 3rd trimesters. If your patient is on an ACE inhibitor or ARB prior to conception:
  - For the treatment of hypertension, discuss the above with the patient and jointly decide to either switch to an alternative antihypertensive prior to conception, or wait until pregnancy is confirmed & then switch.
  - For the prevention/treatment of proteinuria, continue the ACE inhibitor or ARB until conception occurs. Once pregnancy is confirmed, switch to a safer alternative and resume the ACE inhibitor or ABR post-partum.
  - Insulin requirements are typically decreased in the first trimester (may increase risk of hypoglycemia if significant nausea/vomiting) and increase in 2nd and 3rd trimester.
  - Decreased nutritional intake may increase the risk of diabetic ketoacidosis; ketone monitoring is warranted to ensure mother and baby’s nutritional needs are being met.

Late Pregnancy, Delivery and Post-Partum
- Insulin may not be required on the day of delivery and up to 24-48 hours post partum.
- Insulin requirements may increase if antenatal steroids used in preterm labour.
- Maternal hyperglycemia at delivery increases risk of neonatal hyperglycemia.
- Women who have had GDM should be re-evaluated between 6 weeks – 6 months of delivery with a 75g oral glucose tolerance test (OGTT) and be counseled on a healthy lifestyle.

SCREENING Considerations:
- Ophthalmologic exam – pre-conception, 1st trimester, PRN pregnancy & 1st year post partum; nephropathy – pre-conception; blood pressure – target <130/80, measure at every clinic visit; TSH – pre-conception, or early pregnancy.5

![Figure 1. Screening for and diagnosis of GDM](image)