Preexisting and Gestational Diabetes in Pregnancy

FLORENCE M BROWN MD
SEPTEMBER 8, 2018
Objectives

1. Summarize how preconception care and a planned pregnancy reduce maternal and fetal risks.

2. Summarize the maternal, and fetal risks associated with preexisting DM and GDM in pregnancy.

3. Summarize management strategies during pregnancy and postpartum to reduce risks.

4. Summarize 1 step versus 2 step criteria for GDM diagnosis.
Pre-existing Diabetes and Gestational Diabetes affect Pregnancy and Neonatal Outcomes

<table>
<thead>
<tr>
<th>Complication</th>
<th>Pre-existing</th>
<th>GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Preterm Delivery</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cesarean Delivery</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Neonatal Hypoglycemia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Congenital Malformations</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Fetal Demise</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>DM Complications</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
Definition
- Carbohydrate intolerance of varying severity with 1st recognition of onset occurring during pregnancy, excluding overt diabetes.

With 2-step criteria, complicates 4% of all pregnancies. Prevalence varies from 1-14% depending on the population. 

Management of Preexisting Diabetes

- Preconception counseling
- Pregnancy
- Postpartum
Catwoman- What are her risks?

25 yo G1P0 with Type I diabetes since 1998 presents for first endocrine visit at 11 weeks gestation

1. A1c 12.7% 1 month ago
2. High risk PDR OU s/p scattered laser
3. Diabetic nephropathy- urine ACR 1428.0 mcg/mg
4. Hypertension- off ACE-I and on nifedipine
5. Unplanned pregnancy.
Preconception counseling requires a planned pregnancy

– Contraceptive use
– A1c ideally <6.5% without significant hypoglycemia, otherwise <7%.
– Lifestyle - Diet and exercise patterns. If BMI >25 (23 in Asians) aim for 7% weight loss. Refer for MNT.
– Medication list safety. Start PNV.
– Maternal risks/diabetes complications
– High risk behaviors (smoking and alcohol)
– Diabetes in pregnancy specialty care referral.
Preconception counseling
Glucose targets

• Fasting and pre-meal blood glucose: 80-110 mg/dl

• 1-2 hour postprandial blood glucose: 100-155 mg/dl

American Diabetes Association
Diabetes Care 2004 Jan; 27(suppl 1): s76-s78.

Joslin uses 1 hour PP BG: 100-155 mg/dl
Malformation risk vs periconception A1c

Risk of a major or minor anomaly according to periconceptional A1C. *Data are presented as an absolute risk (solid line and blue values) +/- 95% CIs (dashed lines).

Guerin, Diabetes Care 30:1920-1925, 2007
### TABLE 1

**Congenital malformations in infants of diabetic mothers**

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Ratio of incidences*</th>
<th>Gestation age after ovulation(^{8,21,22}) in weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudal Regression</td>
<td>252</td>
<td>3</td>
</tr>
<tr>
<td>Spina Bifida, Hydrocephalus, or other CNS defect</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Anencephalus</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Heart Anomalies</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Transposition of great vessels</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Anal/Rectal Atresia</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Renal Anomalies</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Agenesis</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Cystic kidney</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Ureter duplex</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Situs Inversus</td>
<td>84</td>
<td>4</td>
</tr>
</tbody>
</table>
Trials of Preconception Care for Women with DM:
incidence of malformations % (6-10 fold reduction)

<table>
<thead>
<tr>
<th>Study</th>
<th>Attenders</th>
<th>Nonattenders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuhrman et al 1983</td>
<td>0.8 (1/128)</td>
<td>7.5 (22/292)</td>
</tr>
<tr>
<td>Damn et al 1989</td>
<td>1.0 (2/193)</td>
<td>8.2 (5/61)</td>
</tr>
<tr>
<td>Steel et al 1990</td>
<td>1.4 (2/143)</td>
<td>10.4 (10/96)</td>
</tr>
<tr>
<td>Kitzmiller et al 1991</td>
<td>1.2 (1/84)</td>
<td>10.9 (12/110)</td>
</tr>
<tr>
<td>Wilhoite et al 1993</td>
<td>1.6 (1/62)</td>
<td>6.5 (8/123)</td>
</tr>
</tbody>
</table>
Prenatal vitamin supplementation

• Folic acid 0.4 to 0.8 mg (400-800 µg) to reduce the risk of neural tube defects

• Potassium iodide 150 mcgs – to correct possible iodine deficiency and ensure adequate substrate for maternal and fetal thyroid hormone synthesis.

• USPSTF JAMA 2017 Jan 10;317(2):183-189.
Periconception A1C% vs Perinatal Mortality
Type 1 DM (RR vs normal)

• A1c < 6.9% – perinatal mortality 2.1% (RR 2.8)
• A1c 8.9-10.3% - perinatal mortality 6.3% (RR 8.3)

Reece Am J Obstet Gynecol 1988;159:56-66
### HbA1c Cut-Offs at First Prenatal Visit and the Relative Risk of Preeclampsia

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>% (n) &lt;HbA1c</th>
<th>% (n) ≥HbA1c</th>
<th>Univariate RR (95% CI)</th>
<th>p-value</th>
<th>Multivariable RR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 6.5</td>
<td>48.1 (76)</td>
<td>51.9 (82)</td>
<td>4.63 (1.40, 15.38)</td>
<td>0.01*</td>
<td>4.42 (1.35, 14.47)</td>
<td>0.01*</td>
</tr>
<tr>
<td>≥ 7</td>
<td>67.1 (106)</td>
<td>32.9 (52)</td>
<td>5.30 (2.00, 14.07)</td>
<td>0.001*</td>
<td>5.26 (2.06, 13.41)</td>
<td>0.001*</td>
</tr>
<tr>
<td>≥ 7.5</td>
<td>78.5 (124)</td>
<td>21.5 (34)</td>
<td>5.73 (2.41, 13.66)</td>
<td>&lt;0.0001*</td>
<td>5.60 (2.50, 12.56)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>≥ 8</td>
<td>85.4 (135)</td>
<td>14.6 (23)</td>
<td>4.70 (2.08, 10.64)</td>
<td>0.0002*</td>
<td>4.60 (2.18, 9.69)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

*Controlling for parity and body mass index

- **For every 0.5 increment in A1c% from 6.5 to 8.0 comparing < to ≥ the specified A1c, the relative risk of preeclampsia increases**

## Prematurity, hypertensive complications and prematurity caused by preeclampsia

<table>
<thead>
<tr>
<th>White Class</th>
<th>#premature deliveries (%)</th>
<th># HTN complications (%)</th>
<th>#premature deliveries due to preeclampsia (%)</th>
<th>Total #</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>21 (20.4%)</td>
<td>18 (17.5%)</td>
<td>5 (5.0%)</td>
<td>103</td>
</tr>
<tr>
<td>C</td>
<td>21 (17.4%)</td>
<td>28 (23.1%)</td>
<td>6 (5.0%)</td>
<td>121</td>
</tr>
<tr>
<td>D</td>
<td>26 (25.7%)</td>
<td>31 (30.7%)</td>
<td>7 (6.9%)</td>
<td>101</td>
</tr>
<tr>
<td>F nephropathy</td>
<td>31 (52.2%)</td>
<td>39 (66.1%)</td>
<td>14 (23.7%)</td>
<td>59</td>
</tr>
<tr>
<td>R retinopathy</td>
<td>11 (30.5%)</td>
<td>9 (25.0)</td>
<td>4 (11.1)</td>
<td>36</td>
</tr>
<tr>
<td>Total</td>
<td>110 (26.2)</td>
<td>125 (29.8)</td>
<td>36 (8.6)</td>
<td>420</td>
</tr>
</tbody>
</table>

Descriptors of Fetal Overgrowth

- Macrosomia- birthweight >4000 grams
  - Present in approximately 30-55% offspring

- Large for Gestational Age->90% for birthweight
  - Present in approximately 50% of offspring overall
  - Present in 25% of offspring when pre-delivery A1c<6%
  - Infant birthweight demonstrates a strong shift to the R vs normal.

  - Evers, BMJ. 2004 Apr 17;328(7445):915. Epub 2004 Apr 5
  - James-Todd Hypertens Pregnancy 2016 Jul 2 35(3) 436-446
Non-type 1 diabetic reference population

3,705 infants to mothers with type 1 diabetes

Birth weight standard deviation score

Relative frequency, %
Pederson Hypothesis: hyperglycemia and excess fetal growth

Kjos and Schaeffer-Graf Diabetes Care 30 supp 2 July 2007 p 20
Barrett et.al. Diabetes Care May 2014,37:1484-1493
Pregnancy Affects Maternal Diabetes Complications

- Retinopathy
- Nephropathy
- Severe hypoglycemia
- Beyond scope because less frequent: DKA, CAD, hypertriglyceridemia
Baseline Level of Retinopathy Predicts Risk of Progression During Pregnancy

• Mild non-proliferative (NPDR)
  – Changes during pregnancy are minimal and return to baseline postpartum
• Moderate to severe NPDR- Progression to proliferative retinopathy occurs in 10-25%. Severe NPDR may be stabilized with laser preconception or in the 1st trimester
• Proliferative -High risk of progression. Stabilize preconception.
• Proliferative in remission-rarely associated with reactivation
• Need sequential dilated eye exam or high resolution retinal imaging each trimester and post partum or more frequently, if indicated
• Additional risk factors for activation of retinopathy include: high initial A1c, greater/rapid decrease in A1c, hypertension. Risk may continue up to 1yr PP
  • Adapted from Kitzmiller et.al. Managing Preexisting Diabetes and Pregnancy ADA Technical Reviews and Consensus for Care. Au Brown and Jovanovic, Diabetic Retinopathy and Pregnancy and Table II.23
  • DIEP Diabetes Care, vol 18:5, 1995
  • DCCT NEJM 1993
Microalbuminuria and Nephropathy in Pregnancy

- Urinary albumin excretion rates increase in pregnancy.
  - Return to baseline postpartum.
    - Nephropathy is difficult to distinguish from preeclampsia.
- If GFR is reduced at baseline, may have permanent worsening of kidney disease.

- **Assess baseline serum creatinine and urine ACR to evaluate for underlying kidney disease.**

McCance Diabetologia 32:236-9, 1989
When should ACE-I inhibitors be stopped?

- 2nd and 3rd trimester fetal anuria/oligohydramnios/skeletal defects are well established

- 1st trimester 2 fold increase in malformations but not confirmed in other studies.

- Discontinue preconception in those with microalbuminuria

- Discontinue as soon as pregnancy diagnosed in those with nephropathy or reduced GFR in whom loss of renal protection is a concern.

- Li et.al. BMJ. 2011 Oct 18, 343():d5931
- Porta et.al. Diabetologia. 2011;54:1298–303
## Incidence of Severe Hypoglycemia

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal and Year</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rudolph</td>
<td>Diabetes 1981</td>
<td>6</td>
</tr>
<tr>
<td>Skyler</td>
<td>Diabetes Care 1980</td>
<td>11</td>
</tr>
<tr>
<td>Coustan</td>
<td>JAMA 1986</td>
<td>15-20</td>
</tr>
<tr>
<td>Bergman</td>
<td>NY State J Med 1986</td>
<td>19.2</td>
</tr>
<tr>
<td>Rayburn</td>
<td>Int.J Gyn. Obst. 1986</td>
<td>33</td>
</tr>
<tr>
<td>Kimmerle</td>
<td>Diabetes Care 1992</td>
<td>41</td>
</tr>
</tbody>
</table>
Hypoglycemia in Pregnancy

- “Tight” glucose goals
- Relax goals if hypoglycemia unawareness.
- CGM alarms may help alert to hypoglycemia.
- Always test blood glucose level before driving.
- Teach spouse or partner how to use glucagon.

Type 2 DM Preconception

- Insulin is the only safe and effective treatment in pregnancy. Transition to insulin preconception, ideally.

- Metformin may be continued until pregnancy is diagnosed in women with PCOS or type 2 diabetes and anovulatory infertility.

- Glyburide and metformin are not known teratogens. May be continued until bgs are controlled with insulin. Both cross the placenta and are not effective in controlling bgs in pregnancy.

- GLP-1 agonists, DPP-4 inhibitors, alpha-glucosidase inhibitors, and SGLT2 inhibitors in pregnancy > Inadequate safety

Avoid preconception.
Management of Preexisting Diabetes

- Preconception counseling
- Pregnancy
- Postpartum
Intensive insulin management

- **Basal/bolus approach:**
  - Multiple Daily Injections or
  - Continuous subcutaneous insulin infusion

- **Prandial dosing depends on skill level**
  - Highest skill level: carbohydrate counting and establish insulin/carb ratio.
  - Basic skill: use consistent meal plan for fixed insulin dosing or sliding scale.

- **Analogues**
  - Rapid acting: lispro and aspart B pharmacokinetics offer advantages over regular
  - **Detemir** category B. Detemir non-inferior to NPH in RCT. Glargine- category C, unknown effects related to 6x increased binding to the IGF1 receptor vs human insulin. Does not appear to cross placenta in infusion studies. Most clinical data is from retrospective cohort studies.

- Mathiesen Diabetes Care 2012
- Tennagels, Arch Physiol Biochem 119:1-14 2013
- Pollex. Diabetes Care 2010, 33:29-33
- Pollex Ann Pharmacother 2011,45:9-16
Major Changes in Insulin Requirements Occur in Pregnancy Related to Normal Physiology of Pregnancy

- Late 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester insulin resistance is possibly associated with increasing levels of placental hormones (hPGH) or adipokines (TNF alpha)

- Total daily insulin requirements:
  - Increase 1.34%/week, preconception->9 weeks,
  - Decrease 1.51%/week, 9-16 weeks
  - Increase 5.19%/week, 16-37 weeks

Garcia-Patterson A, etal. Diabetologia 2010
Total daily insulin requirements change throughout pregnancy with T1DM

Open circles - Total daily insulin requirement,
Closed circles - insulin requirements/U/kg,
Closed squares - capillary blood glucose in mm/mol/L.
Most severe hypos occur in weeks 0-16.

Garcia-Patterson A, et.al. Diabetologia 2010
ADA/ACOG Glycemic Targets PEDM +GDM
(mean of normal + SD)

- $F \leq 95$ mg/dl (mean 71 +/- 16 mg/dl 2SD)
- $1 \text{ hr} - \leq 140$ mg/dl (mean 109 +/- 26 mg/dl 2SD)
- $2 \text{ hour} \leq 120$ mg/dl (mean 99 +/- 20 mg/dl 2SD)
- Compared with Joslin targets of $F$ 60-99 mg/dl for preexisting DM, $1\text{hr}$-100-129mg/dl for preexisting and GDM
- A1c <6.0
- No RCTs comparing targets. Targets need to consider normal ranges versus the risk of hypoglycemia in your population (type 1, type 2, GDM).

Hernandez et al Diabetes Care July 2011; 34 1660-1668
ACOG Practice Bulletin #60, 2005
Metzger Diabetes Care 2007;30(Suppl. 2):S251–S260
Management of diabetes during L&D

- Maintain bgs 80-110 mg/dl
- Test bgs hourly until patient has delivered and resumed eating.
- Start IV insulin infusion per L+D protocol if bgs >110 mg/dl or immediately if patient disconnecting from pump.
- Titrate insulin drip as necessary. Stop drip if bg < 70mg/dl. Repeat glucose in ½ hour. Target bgs 80-110 mg antepartum and 100-150 mg/dl post partum.
Postpartum management

• Resume insulin at approx ½ of preconception dose.

• Titrate dose upward over the next 2-14 days as postpartum insulin sensitivity resolves

• Breast feeding may increase insulin sensitivity. Keep snacks nearby.

• L thyroxine doses (if hypothyroid) return to preconception dose.

• F/U 2 weeks for glucose management

• F/U 6 weeks to discuss management of glucose control, concurrent medical conditions, complications and contraception.

Catwoman- What are her risks?

25 yo G1P0 with Type I diabetes since 1998 presents for first endocrine visit at 11 weeks gestation

1. A1c 12.7% 1 month ago
2. High risk PDR OU s/p scattered laser
3. Diabetic nephropathy- urine ACR 1428.0 mcg/mg
4. Hypertension- off ACE-I and on nifedipine
5. Unplanned pregnancy.
Update on Gestational Diabetes

Florence M Brown MD
7/19/2018
7/26/2018
Gestational Diabetes

- Definition: hyperglycemia in pregnancy but not DM.
- Epidemiology/risk factors
- Pathogenesis
- Screening and diagnosis (2 step vs 1 step)
- Treatment and treatment goals
- Risk of future type 2 DM
Patient Nell with GDM

- 34 yo G2P1 without prior hx of GDM
- Dx- at 26 weeks after 2 hour 75 gm OGTT: F 89, 1 hour 197 and 2 hour 156 mg/dl.
- She has received education and nutrition counseling from RN and nutritionist.
- Fhx- + T2DM in father, paternal GM and uncle.
- PE- Preconception Wt 177 lbs (80 kgs), BMI 32, current wt 206 lbs (93 kgs) +acanthosis
- SMBG- Fasting and 1hour postprandial bgs are in target.
High Risk is Defined By ACOG

- Obesity
- Previous history of GDM
- Glycosuria
- Strong family hx of DM (1\textsuperscript{st} degree relative)
- Impaired OGTT or IFG
- Previous baby with > 9 lb birth wt.

Women at high risk should be screened in the first trimester or \textbf{before pregnancy} to rule out diabetes.
In normal pregnancy

• Insulin resistance in the second half of pregnancy is necessary to allow for adequate fuel delivery to the fetus.

• GDM screening done at 24-28 weeks when insulin resistance has occurred and hyperglycemia is usually manifest.

The Diagnosis of GDM is Controversial

- **1 Step method** - fasting 75 gm 2 hour OGTT (F, 1, 2 hour values - GDM ≥ 1 abnormal value) (Proposed by IADPSG, endorsed by ADA, Endo Society, WHO, FIGO)

- **2 Step method** - screening based on historical risk factors or a 1 hour 50 gm GLT (non fasting), if positive -> a fasting 3 hour 100 gm OGTT (F, 1, 2, 3 hour values - GDM ≥ 2 abnormal values) (Endorsed by ACOG, NIH consensus conference), and recently also ADA
The diagnostic thresholds for 100 gm OGTT (2 abnormal values required for GDM)

<table>
<thead>
<tr>
<th>100gm OGTT criteria</th>
<th>NDDG conversion Plasma mg/dl</th>
<th>Carpenter &amp; Coustan Plasma mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>105</td>
<td>95</td>
</tr>
<tr>
<td>1 hour</td>
<td>190</td>
<td>180</td>
</tr>
<tr>
<td>2 hour</td>
<td>165</td>
<td>155</td>
</tr>
<tr>
<td>3 hour</td>
<td>145</td>
<td>140</td>
</tr>
</tbody>
</table>
HAPO – Observational Study

- 23,316 women
- 75 gm OGTT at 24-32 weeks: fasting, 1hr, and 2 hr glucose obtained. These results were blinded.
- Women were excluded from the study and results were unblinded if 2hr >200 mg/dl or if fasting > 105 mg/dl, any <45 mg/dl, random >160 mg/dl
- Only those that stayed blinded were analyzed for the relationship of fasting, 1 hour and 2 hour glucose vs neonatal and pregnancy outcomes.

Maternal Fasting Glucose vs Neonatal Outcomes

Figure 1: Maternal glucose associations with birthweight >90th percentile, cord C-peptide >90th percentile, and percent body fat > 90th percentile (see references 25,26)
Maternal 1 hr Glucose vs Neonatal Outcomes

1 hour plasma glucose

Copyright 2009 ADA. Published online at http://care.diabetesjournals.org/cgi/content/full/dc09-1848/DC1.
Maternal 2 hr Glucose vs Neonatal Outcomes

2 hour plasma glucose

Copyright 2009 ADA. Published online at http://care.diabetesjournals.org/cgi/content/full/dc09-1848/DC1.
All HAPO Outcomes- normal vs 1 abnormal glucose

Table B. Frequency of outcomes when all glucose values are below threshold or any one or more is equal to or above threshold†

<table>
<thead>
<tr>
<th>Outcome</th>
<th>FPG, 1-hr and 2-Hr OGTT values all &lt; threshold</th>
<th>FPG and/or 1-hr and/or 2-hr OGTT values &gt; threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight &gt; 90th percentile</td>
<td>8.3%</td>
<td>16.2%**</td>
</tr>
<tr>
<td>Cord C-peptide &gt; 90th percentile</td>
<td>6.7%</td>
<td>17.5%**</td>
</tr>
<tr>
<td>Percent body fat &gt; 90th percentile</td>
<td>8.5%</td>
<td>16.6%**</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>4.5%</td>
<td>9.1%**</td>
</tr>
<tr>
<td>Preterm delivery (&lt; 37 weeks)</td>
<td>6.4%</td>
<td>9.4%**</td>
</tr>
<tr>
<td>Primary cesarean section</td>
<td>16.8%</td>
<td>24.4%**</td>
</tr>
<tr>
<td>Shoulder dystocia and/or birth injury</td>
<td>1.3%</td>
<td>1.8%*</td>
</tr>
<tr>
<td>Clinical neonatal hypoglycemia</td>
<td>1.9%</td>
<td>2.7%*</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>8.0%</td>
<td>10.0%**</td>
</tr>
<tr>
<td>Intensive neonatal care</td>
<td>7.8%</td>
<td>9.1%*</td>
</tr>
</tbody>
</table>

†Threshold values: FPG > 5.1 mmol/l (92 mg/dl), 1-hr PG > 10.0 mmol/l (180 mg/dl), 2-hr > 8.5 mmol/l (153 mg/dl)

*Difference between groups significant at p < 0.01
**Difference between groups significant at p < 0.001
Prevalence of GDM by Country Using IADPSG Versus Old Criteria

Reported Prevalence of GDM by Country Using IADPSG criteria

Location

By Previous Criteria  By IADPSG  HAPO

Brown, Wyckoff Curr Diab Rep 2017 17:85
Landon 2009- Does Treatment of Mild GDM Make a Difference?

• Study group: 958 women in 24th to 31st week of gestation

• Inclusion criteria: Fasting glucose <95 and 2 or 3 abnormal values on 3-hr OGTT (1-hr >180 or 2-hr >155 or 3-hr >140 mg/dL)

• Randomization: 485 to insulin treatment group; 473 to control group (blinded)

• Treatment group targets: Fasting <95, 2-hr <120 mg/dL

## Results

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth wt</td>
<td>3302 g</td>
<td>3408 g</td>
</tr>
<tr>
<td>Birth wt &gt; 4000 g</td>
<td>5.9%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Fat mass (g)</td>
<td>427</td>
<td>464</td>
</tr>
<tr>
<td>Caesarean delivery</td>
<td>26.9%</td>
<td>33.8%</td>
</tr>
<tr>
<td>Shoulder dystocia</td>
<td>1.5%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Preeclampsia/G HTN</td>
<td>8.6%</td>
<td>13.6%</td>
</tr>
</tbody>
</table>

\( P < 0.001, < 0.001, 0.003, 0.02, 0.02, 0.01, \text{respectively} \)

American Diabetes Association

- Endorsed the IADPSG guidelines in 2011
- “There is emerging observational and retrospective evidence that women diagnosed with the new criteria (even if they would not have been diagnosed with older criteria) have increased rates of poor pregnancy outcomes similar to those of women with GDM by prior criteria”
- Endocrine Society adopted 2013

ACOG- Committee Opinion
September 2011

- Continued to recommend 1-hr 50 g screening test for women with risk factors

- Diagnosis of GDM will still be made by 3-hr 100 g GTT (either NDDG or CC criteria)

- Approximately 18% of women would be diagnosed with GDM based on IADPSG guidelines.

- NIH Consensus Conference concurred.

- ACOG Practice Bulletin 2013 reaffirmed their position
- ADA accepted either 1-step or 2-step testing for GDM


Pathophysiology of GDM is characterized by preconception

- Insulin resistance
- Reduced insulin secretion
- These metabolic defects precede pregnancy and will continue after pregnancy, increasing the risk of future type 2 diabetes.

Buchanan et al. Diabetes Care 30 S105-111, 2007
Kim et al Diabetes Care 25 pp 1862-1868, 2002
Treatment of GDM starts with Lifestyle

- **Diet** – Moderate carb restriction i.e. 30-15-45-15-45-15 grams. Avoid ketonuria. "Healthy Plate counseling"
- Ok to increase healthy carbs, if SBGM in target.
- **Exercise** – walking, low impact activity
- **Self monitoring of blood glucoses** before breakfast and 1-2 hours post meals
- **AM urine ketone monitoring**
  - https://www.hsph.harvard.edu/nutritionsource/healthy-eating-plate/
Medical Management of GDM

- **Insulin**- Is standard of care and endorsed as first line therapy by ADA and ACOG. Does not cross placenta.

- Oral medications glyburide and metformin- never endorsed as first line by ADA are no longer endorsed as first line option by ACOG. They reversed their position July 2017. Both cross placenta.

ACOG Practice Bulletin 137, Gestational Diabetes August 2013
ACOG Practice Bulletin 180, GDM July 2017
# ADA/ACOG Glycemic Targets PEDM +GDM (mean of normal + SD)

- **F** ≤ 95 mg/dl (mean 71 +/- 16 mg/dl 2SD)
- 1 hr- ≤ 140 mg/dl (mean 109 +/- 26 mg/dl 2SD)
- 2 hour ≤ 120 mg/dl (mean 99 +/- 20 mg/dl 2SD)
- Compared with Joslin targets of F 60-99 mg/dl for preexisting DM, 1hr-100-129mg/dl for preexisting and GDM
- **A1c** <6.0
- No RCTs comparing targets. Targets need to consider normal ranges versus the risk of hypoglycemia in your population (type 1, type 2, GDM).

Hernandez et al Diabetes Care July 2011; 34 1660-1668
ACOG Practice Bulletin #60, 2005
Metzger Diabetes Care 2007;30(Suppl. 2):S251–S260
GDM and Fetal Abdominal Circumference

**Figure 2**—Flow chart of “modified” treatment of GDM-based serial ultrasound measurement of fetal AC. Fetal AC measurement is categorized as low-risk (≤75th percentile for gestational age) or high-risk (≥75th percentile for gestational age). When low-risk fetal growth is maintained, glycemic targets can be relaxed. When high-risk fetal growth identified, lower thresholds are used (fasting <80, 2-hour post meal <100-110mg/dl). Diabetes Care 30. Supp 2 S200-205 Kjos and Schaefer-Graf- 2007
Figure 3—Cumulative incidence of diabetes after GDM in five studies (59–65). Adapted from Kim et al. (51).

Kim et al Diabetes Care 25 pp 1862-1868, 2002
Postpartum management GDM

- No insulin required (usually).
- Monitor pre-breakfast and 2 hours post meal blood glucoses for 24 hours.
- Perform **75gm 2 hour OGTT** at 6 weeks post partum and at 1 year and every 3 years. A1c or fasting glucose alternate years.
- Recommend **dietary and exercise** modifications based on Diabetes Prevention Program to reduce future risk. Follow Healthy Plate
- **Target 7% weight reduction below the preconception weight**, If preconception BMI > 25 (>23 for Asians)


Patient Nell with GDM

- 34 yo G2P1 without prior hx of GDM
- Dx- at 26 weeks after 2 hour 75 gm OGTT F 89, 1 hour 197 and 2 hour 156 mg/dl.
- She has received education and nutrition counseling from RN and nutritionist.
- Fhx- + T2DM in father, paternal GM, uncle.
- PE- Preconception Wt 177 lbs (80 kgs), BMI 32, current wt 206 lbs (93 kgs) + acanthosis
- SMBG- Fasting and 1hour postprandial bgs are in target.
Check List For Providers

- **Identify** high risk women of childbearing age in your cohort for preconception counseling.
- **Check** contraception use every visit.
- **Counsel** on reduce the risk of adverse outcomes especially birth defects, if A1c is elevated.
- **Refer** for medical nutrition counseling and weight loss goal of 7% if BMI is above target.
- **Refer** for urgent specialty care <1 week appointment, If unplanned pregnancy. Discontinue statins, ACE inhibitors.
- **Screen** for abnormal glucose metabolism yearly, if prior GDM. **Treat** with lifestyle management or metformin for prevention.
Diabetes in Pregnancy Program

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