

Diabetes in Pregnancy Update

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Objectives

- Examine HAPO study results
- Review diagnostic criteria
- Describe new Alaska Area guidelines
- Discuss oral hypoglycemic therapy
- Discuss insulin therapy
- Discuss long term follow-up

Hyperglycemia and Pregnancy Outcomes

- 25,505 pregnant women
 - 15 centers in 9 countries
 - 75-g OGTT at 24 to 32 weeks
 - Blinded if.....
 - Fasting plasma glucose < 105 mg and
 - 2-hour plasma glucose < 200 mg
-
- N Engl J Med. 2008 May 8;358(19):1991-2002

HAPO Primary outcomes

- Birth weight > 90th percentile
- Primary cesarean delivery
- Clinically neonatal hypoglycemia
- Cord-blood C-peptide > 90th percentile

C-peptide = proxy for fetal insulinemia

- Primary outcome variable: the higher the cord, insulin the more likely that mother had high glucose which crossed to the fetus
- ~15% of cord specimens will hemolyze
- Hemolysis lowers plasma insulin concentrations, whereas it does not affect c-peptide
- Strong correlation between c-peptide and insulin

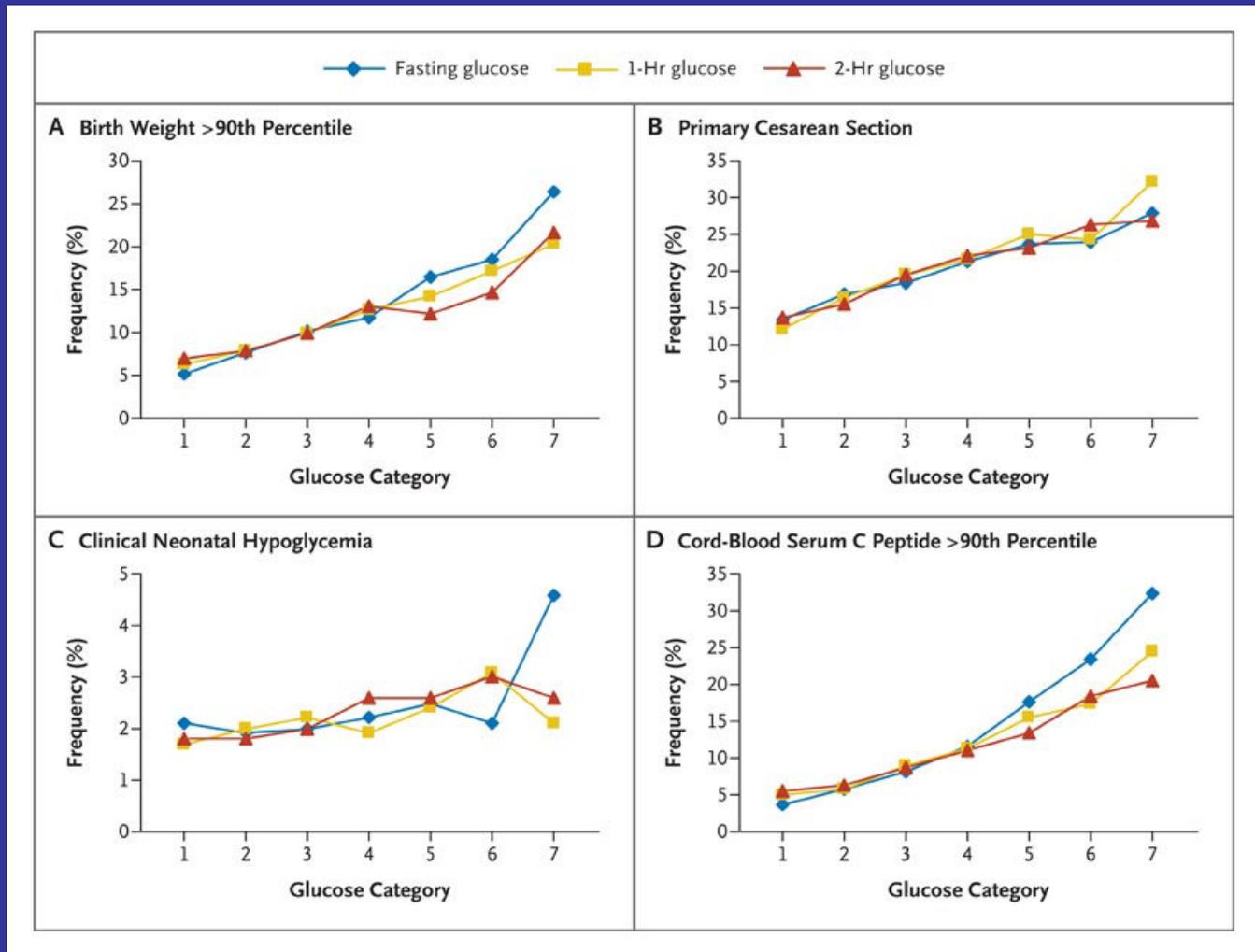
HAPO Secondary outcomes

- Delivery < 37 weeks
- Shoulder dystocia
- Birth injury
- Intensive neonatal care
- Hyperbilirubinemia
- Preeclampsia

HAPO Results

- 23,316 participants with blinded data
- Fasting glucose 6.9 mmol/L 1 SD
- 1-hour 30.9 mmol/L 1 SD
- 2-hour 23.5 mmol/L 1 SD

Frequency of Primary Outcomes across the Glucose Categories



The HAPO Study Cooperative Research Group. N Engl J Med 2008;358:1991-2002

IHS Division of Diabetes



The NEW ENGLAND JOURNAL of MEDICINE

HAPO Results

- No obvious thresholds at which risks increased
- Significant associations were also observed for secondary outcomes, though weaker

HAPO CONCLUSIONS

Strong, continuous associations

Maternal glucose levels below those diagnostic of diabetes

- Birth weight
- Cord-blood serum C-peptide levels

HAPO plus 3 factors... voila...

- Crowther CA and Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group
- Landon MB and National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network
- International Association of Diabetes and Pregnancy Study Groups

Crowther et al 2005

- RCT 1000 women
- Reduced serious perinatal complications (defined as death, shoulder dystocia, bone fracture, and nerve palsy)
 - admission to the neonatal nursery, jaundice requiring phototherapy,
 - induction of labor, cesarean birth, and maternal anxiety, depression, and health status.
- N Engl J Med. 2005;352(24):2477-86

Landon et al 2009

- A multicenter, randomized trial of treatment for mild gestational diabetes
- RCT 958 women
- Reduced the risks of fetal overgrowth, shoulder dystocia, cesarean delivery, and hypertensive disorders
- N Engl J Med. 2009 Oct 1;361(14):1339-48.

IADPSG

- International Association of Diabetes and Pregnancy Study Groups
- Pasadena: June 11-13, 2008
- International Workshop Conference on Gestational Diabetes Diagnosis and Classification

IADPSG criteria

- First visit: r/o overt diabetes
- Hgb A1C > 6.5 %
- Random glucose > 200 mg/dL**
- Fasting glucose >126 mg/dL*

*...but if FBS > 92 mg/dL then GDM

**Needs a confirmatory value

IADPSG criteria

- 24-28 wk OGTT, 75 gm
- Only one value needed

- FBS 92 mg/dL
- 1 hr 180 mg/dL
- 2 hr 153 mg/dL

Standards of Medical Care in Diabetes—

2011

Table 6

Screening for and diagnosis of GDM

Perform a 75-g OGTT, with plasma glucose measurement fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are exceeded:

- Fasting ≥ 92 mg/dl (5.1 mmol/l)
- 1 h ≥ 180 mg/dl (10.0 mmol/l)
- 2 h ≥ 153 mg/dl (8.5 mmol/l)

This Article

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What's this?



10/15/10 njm

ANMC OB/GYN Service Diabetes Mellitus in Pregnancy Screening and Management Guidelines

I. Introduction

In the last 2 generations diabetes in pregnancy has increased significantly in Alaska Natives. Diabetes can be associated with morbidity and mortality for both the pregnant patient and her offspring. Management of diabetes in pregnancy offers a unique opportunity to positively impact both patients' lives.

With the publication of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study and the subsequent International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria we now have randomized controlled data to guide management. While awaiting other

Guidelines available www.ihs.gov

- <http://www.ihs.gov/NonMedicalPrograms/NC4/Documents/DMPreg.doc>

“At risk”

- ...if Hgb A1C 5.7- 6.4 %
- ...if RBS 140-199 mg/dL
- The voila.... just do a FBS....
- ...if ≥ 92 mg/dL you can treat as GDM...

Pro(s) and Con(s)

- 1st prenatal screen is easy
- 3rd trimester screen does not lose ~20+% to f/u due to 2 step process
- Diagnoses more patients = good long term

Pro(s) and Con(s)

- Cons
 - Diagnoses more patients = bad (below)
 - More resources are utilized post Dx

Prevalence

GROUP	RATE GDM%
U.S.	4.0-7.0
Hispanic	3.0
Sacaton	10.0
GIMC	7.0
White River	9.0
Zuni	16.0
Bemidji	8.0
Bethel	6.1

Complications of Diabetes in Pregnancy

- GDM
 - Macrosomia and related problems (maternal and fetal)
- Insulin Requiring Diabetes
 - Anomalies
 - Macrosomia
 - Placental insufficiency
 - IUGR
 - Fetal Compromise

If Abn OGTT, then GDM

- Dietary consult
- Exercise consult
- Home glucose monitoring

GDM Classification: A1 vs A2

- FBS > 95 mg/dl
- 1 hr pp > 130 mg/dl
- 2 hr pp > 120 mg/dl

Management

- Management of pre-gestational diabetes and insulin requiring GDM is more intensive because of increased risk to the fetus
- Approximately 90% of diabetics in pregnancy are non-insulin requiring

GDM - Initial Management

- Diet
 - Fulfill minimum requirements for pregnancy
 - Culturally appropriate
 - Restrict carbohydrates to 35-45% of total caloric intake
 - Utilize complex carbohydrates
 - Level C recommendation

Appendix E

Traditional Diabetes Traditional Foods Meal Plan with Milk

Gestational Diabetes Meal Plan with Milk

This food plan shows different food groups as well as how to eat from each food group. One sample food plan is shown. It contains about 2000-2,200 calories.

	Example	Portions
<u>st</u>		
	Whole wheat toast	1 slice
	Moose/Caribou/fish or egg	2 ounces or 1 egg
	Margarine	1 teaspoon
	Skim milk (or 2%)	1 cup (8 ounces)
	Small Banana or canned fruit (in it' own juice)	1 or 1/2 cup (4 ounces)
	Whole wheat bread	2 slices
	Fish	2 ounces

Initial Management

EXERCISE

Lowers FBS and post prandial levels

- ◆ Optimal type, duration and frequency unclear
- ◆ Aerobic, 20 min, 3x/week
- ◆ Level I data

Appendix F

Exercise guidelines to improve glucose control

Type of activities:

Aerobic activities such as walking, stationary cycling, or swimming

Frequency:

At least 3 days per week

Duration:

20-45 minutes per session

Intensity:

Moderate. The “talk-sing test” may be used – the patient should be able to talk while exercising; if she can sing, the pace can be increased. If using rating of perceived exertion (RPE) exertion level should feel “fairly light” to “somewhat hard”.

Patient should warm-up before and cool down after exercise, drink plenty of water, have snacks nearby if needed.

Initial exercise consult:

Assessment of current physical activities and level of readiness for exercise

Education/Information on exercise and GDM

Individualized exercise plan

Supervised exercise:

Measure blood glucose pre and post exercise

Exercise on treadmill and/or recumbent cycle

Monitor perceived exertion

Monitor blood pressure and/or heart rate as needed

GDM A1 - Followup

Glucose Monitoring - Home vs Clinic

- Initiate insulin if FBS >95, 2hr > 120

Fetal kick counts

Repeat Ultrasound at 28-32 weeks

AC > 70 % = possible Tx

Antepartum testing at 40 weeks

Deliver 40-41 weeks

Medication Requiring - Initial

- Diet
- Exercise
- Assess renal function (Level B)
- Eye exam (Level B)
- Education
- Ultrasound
- ? EKG, HgAlc
- Insulin vs oral agent

Pharmacologic Therapy

- Goal is euglycemia
 - Home monitoring is essential
 - FBS < 95 mg/dL
 - 2 hours post prandial < 120 mg/dL
 - 1 hour pp < 130 mg/dL
- (Level I data)

GDM Class A2

- Glyburide
- Metformin
- Insulin

Oral Agents

- Glyburide
 - Single RCT indicating it is a reasonable treatment for insulin requiring GDM (Langer et al, NEJM, 10/19/2000)
- Multiple Small Case Control Studies, Case Reports
 - Historical
 - South Africa
 - United Kingdom, rural

Metformin

- Start low, move up slowly
- Start at 250 mg / day
- Goal = 1500 mg / day

- RCT 751 women

- Rowan JA et al N Engl J Med. 2008; 358(19): 2003-15

Oral agents

- Systematic review by Johns Hopkins University Evidence-based Practice Center for AHRQ
 - maternal glucose levels did not differ
 - there was no evidence of any adverse maternal or neonatal outcome

Oral agents

-BUT the ADA and the ACOG do not endorse oral anti-hyperglycemic agents during pregnancy yet
- ...and are NOT approved by FDA yet
(please document this in chart)

Pharmacologic Therapy

- Initiation of insulin therapy
 - Single dose of long acting
(e.g., 20u NPH), or
 - 0.7 units/kg in divided doses
(2/3 and 1/3)

Long acting analogs

- Insulin glargine, insulin detemir
- Not been studied extensively in pregnancy
- A multinational trial on the safety and efficacy of insulin detemir for the treatment of type 1 diabetic women is almost complete

GDM Class A2

- Visits q 2-4 weeks till 36 weeks
- Visits q wk after 36 weeks
- Antenatal testing*
 - NST 2x/wk and AFI q wk
- Cervical ripening at 38 weeks

- *If great control....kick counts till 36 wks

Intrapartum Management

- GDM - Non-medication requiring
 - Routine
- Medication requiring
 - Goal is euglycemia (60-90 mg/dL) to avoid neonatal complications
 - Monitor q 1-4 hours
 - Insulin / dextrose as needed

Post Partum - General Concepts

- Non pregnant “normal” levels higher
- “Honeymoon” period - insulin requirements markedly decreased
- Lactation has beneficial effect on glucose tolerance and subsequent development of type 2 diabetes

Post Partum

- Lactation
- Lactation
- Lactation
- Lactation

Immediate Post Partum

- Non-medication requiring
 - Routine
- Medication requiring
 - Monitor FBS, 2° PP
 - Reinstigate oral agent conservatively
 - Follow-up in 1-2 wks to adjust insulin / change to oral hypoglycemic

Post Partum - 6 weeks

- ◆ Gold standard

- ◆ 75 gm, 2 hr OGTT

- ▶ Fasting ≥ 126 mg/dL and/or 2 hr ≥ 200 mg/dl
 - ▶ Impaired fasting glucose > 100 and $< 126^*$
 - ▶ Impaired glucose tolerance > 140 and $< 200^*$
-
- ▶ * Pre-diabetes

GDM: Incidence of type 2 DM

- > 70% up to 28 years
- Races progress at similar rates
- Incidence increased markedly in first 5 yrs
- Plateau after 10 yrs
- FBS during pregnancy most commonly associated with future risk

- Kim C et al Diabetes Care. 2002 Oct;25(10):1862-8

Post Partum

Alternative, slightly less accurate

◆ FBS

- ▶ $\geq 126 \times 2$ - Diabetes
- ▶ 100-125 - Impaired fasting glucose
▶ (Pre-diabetes)
- ▶ < 100 - Normal

Post Partum - Long Term

- GDM: q 3 year glucose screening
- Lifestyle modification
- Preconceptual counseling
- Contraception
- Offspring risks

Family Planning

- OCPs
- Depo-Provera
- IUD
- All barrier methods
- Sterilization

Pre-conception counseling

- Folic acid
- Maintain euglycemia / SABs (Level B)
- Avoid teratogens
- Healthy behavior
- Safer sex

Good review

- First Evidence-Based Criteria for Diagnosis of Gestational Diabetes
- http://www.ihs.gov/MedicalPrograms/MCH/index.cfm?module=whn_5_1

What's next ?

- Await ACOG's decision on Dx criteria
- Lantus trial pending
- "At risk" group
- ?Early intervention if FBS not > 92 mg/dL but at risk Hgb A1c or RBS