Early Gestational Diabetes Screening in Gravid Obese Women

(EGGO)

Protocol

(Version 1.1; 02.17.2014)

Study Procedures

1. **Screening**. Records of health clinic patients will be reviewed by trained research staff to identify eligible patients. Eligible patients will receive a letter and/or phone call notifying them of their eligibility and asking them to participate. Trained research staff will be available at the OB Complications clinic and ultrasound to **screen** and **consent** patients. A screening log or form will be used to track all patients approached for the study. Women will be randomized at the time of consent. At the time of consent, women will sign a maternal/infant medical record release which will be faxed to any hospitals to obtain records for review if necessary.
2. **Randomization**. A confidential, computer-generated simple randomization scheme will be prepared by a designated study biostatistician. Randomization will be stratified by morbid obesity (BMI>40.0. Women will be randomized after they give consent by pulling the next sequential envelope from the participant's BMI group that will disclose whether the participant is assigned to early or routine timing of the GDM screen.
3. **Gestational Diabetes Screening**.
    a. **Early Screening Group**.
        i. Women assigned to "early screening" will complete the BSST (50-g glucose load) between 14 weeks, 0 days gestation and 20 weeks, 0 days gestation. If the test cannot be completed due to nausea or vomiting, the patient may choose to re-schedule another attempt prior to 20 weeks, 0 days or she may choose to withdraw from the study.
            1. If a participant is between 14 weeks, 0 days and 20 weeks, 0 days at the time of randomization she may:
                1. Choose to undergo BSST at the time of randomization in OBCC clinic. Add EGGO to her problem list with a message that she was randomized to early screening & the date of completion of the BSST.
                2. Choose to undergo BSST at next appointment at her local clinic. If she chooses this option, place a message in IMPACT and EGGO to her problem list with her randomization group. This will notify her provider to complete the BSST at the next visit prior to 18 weeks.
        ii. At the time of the BSST, a purple and gold top tube will be drawn for HbA1c & Glycomark (refer to baseline procedures below). These specimens will be labeled with the patient name plate and sent to the OBGYN lab for testing.
        iii. In those who are not diagnosed with GDM at the early screen, repeat testing will be performed at 24-28 weeks.
    b. **Routine Screening Group.**
        i. Women assigned to routine screening will have a blood draw for HbA1c and Glycomark between 14 weeks, 0 days and 20 weeks, 0 days gestation.

- If HbA1c≥6.3% in the routine screening group, the result will be unblinded and the clinician informed. These women will subsequently enter into routine GDM care with dietary counseling and patterned blood sugars.
- If the patient is between 14 weeks, 0 days and 20 weeks, 0 days this blood draw may be performed at the enrollment visit. Otherwise, may be done in clinic with routine prenatal labs.

ii. Women assigned to "routine screening" will undergo the 1-hour, 50-g glucose load (BSST) between 24 weeks, 0 days and 28 weeks, 0 days gestation. At the time of the BSST, a purple & gold top tube for HbA1c & Glycomark will be drawn (see baseline procedures below).

4. Results of Glucose screening tests

a. Women whose BSST is ≥135 mg/dL, will be scheduled to undergo diagnostic testing with a 3-hour GTT (100-g glucose load). The currently used criteria to diagnose GDM (Carpenter Coustan criteria) will be used to diagnose GDM. By these criteria, a woman must have 2 elevated blood sugar values at either of the following timepoints and values:

1. Fasting ≥95 mg/dL
2. 1-hour ≥180 mg/dL
3. 2-hour ≥155 mg/dL
4. 3-hour ≥140 mg/dL

b. The attending physician will review the three-hour GTT results to confirm the diagnosis of GDM.

c. Women who have a BSST>200 will have a fasting blood sugar checked prior to undergoing a 3-hour GTT. If the fasting blood sugar <126 mg/dL, the patient will proceed with a 3-hour GTT. If the fasting blood sugar ≥126 mg/dL, the diagnosis of GDM will be made.

d. Women who are not diagnosed with GDM between 14-20 weeks (i.e. women who have a normal 1-hour BSST or who have an elevated 1-hour BSST but a normal 3-hour GTT) will repeat the 1-hour BSST at 24-28 weeks. At the time of the repeat BSST, a purple & red top tube for HbA1c & Glycomark will be drawn (see baseline procedures below). .

i. Women who are diagnosed with GDM will enter into routine GDM care with dietary counseling and patterned blood sugars. A purple & gold top tube for HbA1c & Glycomark will be drawn between 24-28weeks, and 0 days gestation (see baseline procedures below).

ii. Women who are not diagnosed with GDM (i.e. women who have a normal 1-hour BSST or who have an elevated 1-hour BSST but a normal 3-hour GTT) will continue routine prenatal care.
iii. Women who are diagnosed with GDM will enter into routine GDM care with dietary counseling and patterned blood sugars.

5. Baseline Procedures

- Measurement of height, without shoes, at time of enrollment.
- Record self-reported prepregnancy weight.
- All women will have a blood draw for HbA1c and Glycomark between 14 weeks, 0 days and 20 weeks, 0 days gestation. The blood for HbA1c should be collected in a purple top tube (3mL). The blood for Glycomark should be collected in a gold top tube (3mL).
    - Women undergoing early GDM screening may have these blood samples drawn at the time of the blood draw for the 1-hour BSST.
    - Women randomized to routine screening may have these blood samples drawn at the time of randomization if between 14 weeks, 0 days and 20 week, 0 days. Otherwise, they may have the blood drawn at their clinic at an appropriate time (i.e. at the time of other routine prenatal lab draws).
    - Samples will be labeled with patient name plate for transport to OBGYN lab.
    - Samples may be stored at room temperature or 4°C (refrigerated) for up to 7 days.
- All women will have a blood draw for HbA1c and Glycomark between 24 weeks, 0 days and 28 weeks, 0 days gestation. The blood for HbA1c should be collected in a purple top tube (3mL). The blood for Glycomark should be collected in a gold top tube (3mL).
    - This blood draw may be performed at the time of the 1-hour BSST.
    - Women diagnosed with GDM prior to 24-28 weeks may have the blood drawn in clinic at the appropriate gestational age, in conjunction with routine prenatal lab draws or separately.
    - Samples will be labeled with patient name plate for transport to OBGYN lab.
    - Samples may be stored at room temperature or 4°C (refrigerated) for up to 7 days.
- Trained and experienced research staff in obstetric and perinatal outcomes abstraction will be responsible for all research data abstraction from patient medical records.
- Maternal outcomes will be ascertained in the hospital following delivery and at the routinely scheduled follow-up visit at 4-6 weeks after delivery.
- Newborn outcomes will be ascertained until 6 weeks after delivery through maternal questioning regarding re-admission. Readmissions for infants will be validated through medical review.

6. Follow-up

a. Women with gestational diabetes will be contacted prior to their appointment by either phone or letter to remind them to come to their post-partum visit prepared for the fasting, 2-hour, 75-g glucose tolerance test.

b. Women diagnosed with gestational diabetes will undergo a 2-hour, 75-g glucose tolerance test at the time of their post-partum visit at OBCC or resident continuity clinic. They will receive $10 for undergoing this testing.

c. All women will be asked whether they or their infant have been re-admitted to the hospital since the time of discharge and the reason for admission. Permission will be obtained to request records for re-admission diagnoses.

7. Outcome Measures

The primary outcome will be a composite outcome of macrosomia (birth weight >4000g), primary cesarean, gestational hypertension or preeclampsia, shoulder dystocia, neonatal hyperbilirubinemia, and neonatal hypoglycemia. Each of these outcomes will also be evaluated individually as secondary outcomes. Additional secondary outcomes will include premature delivery (<37wks).

a. Macrosomia: Will be defined by measurement of infant birth weight. Macrosomia is a birth weight >4000 g.

b. Primary cesarean: A primary cesarean delivery for any indication will be considered as having the outcome of interest.

c. Gestational hypertension: Defined by systolic blood pressure ≥140 or diastolic blood pressure ≥90 without proteinuria (urine protein/creatinine ratio <0.19 or 24-hour urine protein <300 mg).

d. Preeclampsia: Defined by systolic blood pressure ≥140 or diastolic blood pressure ≥90 with proteinuria (urine protein/creatinine ratio ≥0.19 or 24-hour urine protein ≥300 mg). Preeclampsia diagnosis will also be refined by mild or severe. Severe preeclampsia will be defined as systolic blood pressure ≥160, diastolic blood pressure ≥110, proteinuria ≥5000 mg in 24 hours or 3+ urine dip, platelets <150, AST >60, oliguria (<500 mL urine/ 24 hours), pulmonary edema, creatinine >1.0,.

e. Shoulder dystocia: As documented by delivering physician; defined as requiring more than routine downward traction to achieve delivery of anterior shoulder. The length of the shoulder dystocia and maneuvers required to relieve the shoulder dystocia will be documented.

f. Neonatal hyperbilirubinemia: Neonatal bilirubin levels will be recorded. Hyperbilirubinemia will be defined >95th percentile gestational age and hour of life. The treatment of hyperbilirubinemia (i.e. phototherapy) will also be recorded.

g. Neonatal hypoglycemia. Blood sugar levels will be abstracted from neonatal charts. Neonatal hypoglycemia will be defined as blood sugar <35mg/dL.

8. Data Collection Form Definitions

a. Randomization Form
    i. Age at the time of presentation
    ii. Body mass index as defined by self-reported pre-pregnancy weight & measured height
    iii. Gestational age <20 weeks, 0 days as defined by earliest documented ultrasound
    iv. Known history of diabetes mellitus by patient report or as documented in clinical records
    v. Major medical illness
        1. Chronic/daily prednisone use
        2. On home oxygen
        3. Prior cardiac surgery
        4. History of cardiomyopathy, valvular stenosis, pulmonary hypertension
        5. History of any transplanted organ
        6. HIV/AIDS
        7. Hemoglobinopathy (i.e. sickle cell disease)

        Conditions not considered a major medical illness:

            1. Chronic hypertension
            2. Asthma (unless requiring prednisone on daily basis)
            3. Obstructive sleep apnea (unless requiring home oxygen)
    vi. Unable to provide informed consent
        1. Language barrier
        2. Prisoner
        3. Mental illness
        4. Judgment of person performing enrollment
    vii. Known fetal anomalies
        1. Structural anomalies (heart defect, brain defect, renal anomaly, abdominal wall defect) or known fetal aneuploidy by karyotype or non-invasive prenatal diagnosis
        2. Soft markers of aneuploidy are not exclusion criteria (echogenic intracardiac focus, choroid plexus cyst, renal pelvis dilation/pyelectasis)
    viii. History of bariatric surgery
        1. Either banding procedure or Roux-en-Y
    ix. Multifetal gestation
    x. Prior cesarean
b. Enrollment Form
    i. Measured height without shoes

ii. Self-reported pregnancy weight obtained from patient interview at time of enrollment
iii. History may be obtained from patient directly or from chart
iv. Exam at time of enrollment

c. Diabetes Testing Form
    i. Document Randomization group
    ii. Document date and value of BSST, GTT, HbA1c, and Glycomark

d. Prenatal Care Data Collection Form
    i. Document whether exclusion criteria developed during course of prenatal care
    ii. Record number of prenatal visits and date, weight, and blood pressure each visit.
    iii. Document date, indication, estimated fetal weight, and amniotic fluid index of each ultrasound.
    iv. Document date and type of antenatal testing performed, & indication for test.
    v. Document all medications prescribed for gestational diabetes. Date started, the starting dose & frequency, the stop date, and the highest dose reached.
    vi. Review other medications and document that there are no changes in medications or update medication list

e. Blood Sugar logs
    i. Record blood sugar logs patient provided. Date, fasting blood sugar, post-prandial blood sugar after each meal, and 21:00 & 3:00 AM blood sugar if documented.

f. Delivery Data Collection Form
    i. Date of admission
    ii. Admitting diagnosis as documented by admitting physician history & physical
    iii. Admission vital signs and labs as documented by the first vital signs and labs obtained on day of admission
    iv. Gestational diabetes type
    v. Blood sugar log & insulin drip as per IMPACT records
    vi. Type of labor as documented by admitting physician history and physical
    vii. Indication for induction of labor based on documentation by admitting physician history & physical
    viii. Indication for scheduled cesarean as documented by admitting physician history & physical
    ix. Medications received during labor: Check all that apply. Any medication received between the time of admission and delivery should be checked.
    x. Record the mode of delivery, indication for operative delivery, shoulder dystocia, laceration/episiotomy, as documented by physician labor and delivery note. If information not documented by physician labor and delivery note, use nursing notes to complete information.

xi. Record arterial and venous blood gases
xii. Post-partum hematocrit – Either spun hematocrit or hematocrit from CBC at 12 hours post-delivery.
xiii. Endometritis as documented by caring physician.

g. Neonatal Form
    i. Highest level of neonatal resuscitation in delivery room as documented by caring pediatricians
    ii. Admitting diagnosis for infant to nursery as documented by pediatricians admission note
    iii. Cause of death as documented by expiration summary
    iv. Neonatal injuries as documented by pediatrics admission note & daily notes prior to discharge
    v. Method of feeding as documented by nursing notes/pediatricians notes
h. Post Partum
    i. Readmission of mother to hospital after initial discharge – obtain by questioning mother and obtain confirmation with records request
    ii. Readmission of infant to hospital after initial discharge – obtain by questioning mother and obtain confirmation with records request