

Managing Diabetes Before, During, and After Pregnancy

This program is supported by an educational grant from Novo Nordisk Inc. It has been accredited by AADE for pharmacists, nurses, and dietitians.

This program, *Managing Diabetes Before, During, and After Pregnancy*, includes information on preconception counseling, diagnosis, and treatment, as well as follow-up care, for women with type 1 or type 2 diabetes, and for those who develop gestational diabetes.

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The following program is a taped presentation by Tanya Engel. Tanya Engel, BS, RN, CDE is a diabetes nurse and coordinator at Easton Hospital, Easton, Pennsylvania where she provides both inpatient and outpatient diabetes education. She has been a certified diabetes educator for over 12 years, working mainly in outpatient diabetes management programs in New Jersey and Pennsylvania. In addition to her role at Easton Hospital, she is also a certified insulin pump trainer for many of the major manufacturers.

Ms. Engel is also certified in inpatient obstetric nursing and, prior to her positions as a diabetes educator, worked in the obstetrical area. Her experience in obstetrics included both primary and tertiary settings in New Jersey and Florida.

Combining her obstetrical and diabetes skills has allowed Ms. Engel a unique perspective while working with high-risk pregnancies in women with diabetes.

Goal and Learning Objectives

Goal:

Provide information on the management of diabetes before, during, and after pregnancy

Objectives:

- Explain assessments associated with preconception care and counseling
- Define recommended screening guidelines for gestational diabetes (GDM)
- Describe changes in metabolism during pregnancy
- Identify three potential fetal complications associated with uncontrolled diabetes
- State two goals for diabetes management during pregnancy

The overall goal of this program is to provide information on the management of diabetes before, during, and after pregnancy.

By the end of the program you will be able to explain assessments associated with preconception care and counseling, define recommended screening guidelines for gestational diabetes, describe changes in metabolism during pregnancy, identify three potential fetal complications associated with uncontrolled diabetes, and state two goals for diabetes management during pregnancy.

Overview

- Prevalence and impact
- Preexisting type 1 or type 2 diabetes
- Gestational diabetes (GDM)
- Metabolic demands of pregnancy
- Management issues
- Fetal monitoring and congenital anomalies
- Postpartum care and follow-up
- Recommendations and summary

We will review the prevalence and impact of diabetes on pregnancy, targeting preexisting diabetes and specifically the issues related to preconception planning, the need for careful assessment, and identifying potential risks.

Gestational diabetes and the risk factors for developing this common complication of pregnancy, the screening criteria for identifying at-risk women, and the need for glucose testing will then be discussed.

In addition, we will examine the metabolic demands of pregnancy.

After discussing these topics, we will then address management issues including mechanisms for monitoring maternal and fetal health, recommended diet and lifestyle issues, and the timely use of insulin for glycemic control.

We will then discuss the options for fetal monitoring and the risks of congenital anomalies. Postpartum follow-up, including treatment and the need for further testing, will be addressed.

And then finally we will summarize the recommendations.

Prevalence and Impact

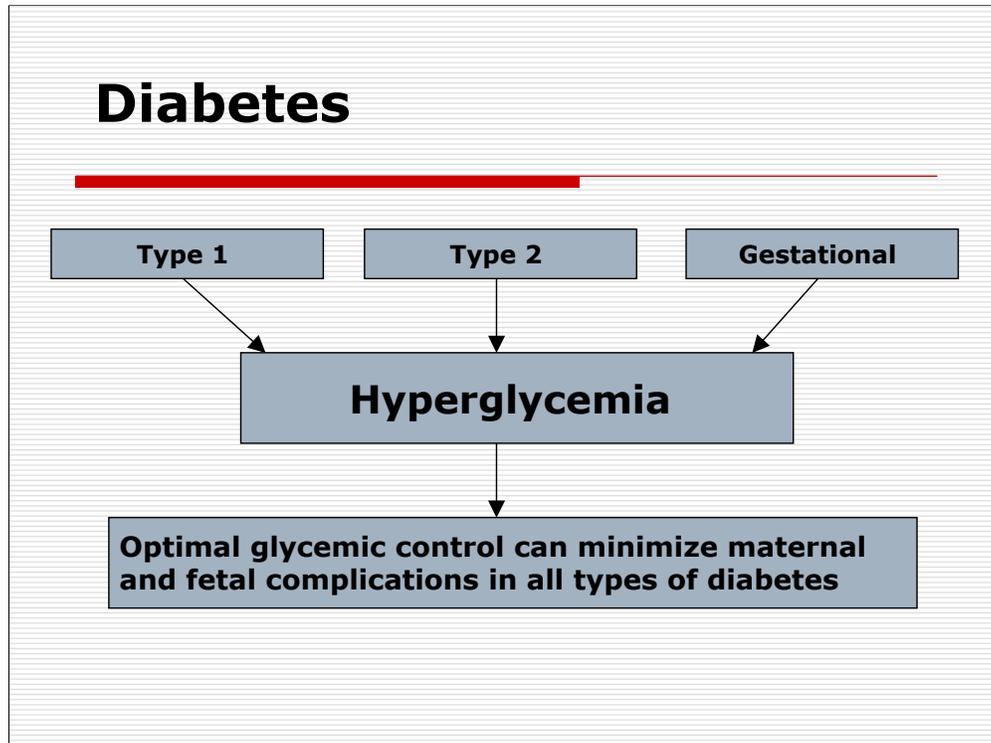
- Diabetes – most prevalent chronic disease in pregnant population
- 7% of all pregnancies are complicated by gestational diabetes, resulting in over 200,000 cases annually
- Infant mortality rate (associated with diabetes) decreased
 - 25% in 1960s
 - 2% in 1980
- Congenital malformations still leading cause of mortality and morbidity in infants of mothers with diabetes
- Unplanned pregnancies occur in 2/3 of women with preexisting diabetes

Let's start by reviewing the impact of diabetes in pregnancy.

Diabetes is the most prevalent chronic disease in the pregnant population. Gestational diabetes complicates 7% of all pregnancies, resulting in over 200,000 cases annually. Although, infant mortality rates due to diabetes-related complications have decreased from 25% in the 1960s to 2% in the 1980s, major congenital malformations remain the leading cause of mortality and morbidity in infants of mothers with diabetes.

These birth defects are associated with uncontrolled blood glucose levels in women with type 1 and type 2 diabetes: a 2%–5% increased risk when the A1C is moderately elevated and a 20%–40% increased risk when the A1C is markedly elevated.

In an effort to decrease the more than 65% of unplanned pregnancies in women with preexisting diabetes, the American Diabetes Association currently recommends that counseling for all women of child-bearing age be included in their routine diabetes medical management and education.



Preexisting diabetes is type 1 or type 2 diabetes that is diagnosed prior to pregnancy. Type 1 diabetes is generally caused by autoimmune destruction of beta cells and results in a virtually absolute insulin deficiency, requiring exogenous insulin to prevent ketosis and to sustain life. Type 2 diabetes is a heterogeneous metabolic dysfunction involving defects in both insulin secretion and tissue sensitivity to insulin.

Gestational diabetes is defined as any diabetes diagnosed during pregnancy. The main issue in gestational diabetes is carbohydrate intolerance of varying degrees with onset or first recognition during pregnancy.

Four percent of women diagnosed with gestational diabetes actually have previously unrecognized type 2 diabetes and more than 50% will develop type 2 diabetes later in life.

Regardless of the type of diabetes, the end result is hyperglycemia.

A pregnant woman with diabetes has a significantly increased risk of maternal and fetal/neonatal morbidity and mortality if glucose levels are not well controlled. Co-morbidities such as hypertension, dyslipidemia, and others need to be managed concurrently to maximize the potential for a positive outcome for both mother and child.

Improved Care

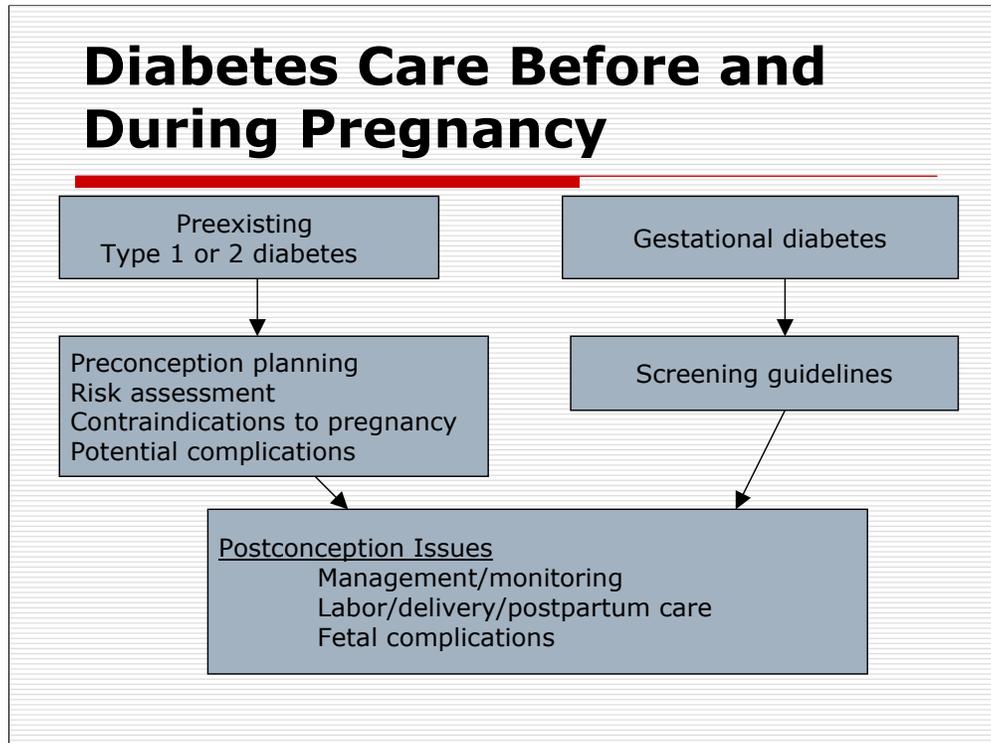
- ❑ Optimal metabolic control before and during pregnancy is essential for a successful outcome
- ❑ Advances in biochemical and electronic monitoring techniques have markedly improved maternal and fetal care and well-being
- ❑ Multidisciplinary team approach

Optimal metabolic control before and during pregnancy is essential for a successful outcome and to minimize the risk of fetal malformations or neonatal complications.

Advances in biochemical and electronic monitoring techniques have markedly improved maternal and fetal care, and enhanced well-being during a pregnancy complicated by diabetes. The reduction in fetal mortality is due in part to modern methods of fetal monitoring, the introduction of neonatal intensive care units, and improved glycemic control through intensified insulin therapy protocols.

A team approach to care that reinforces the importance of planning future pregnancies, and encourages optimal blood glucose control before and during pregnancy is critical. In addition, management of other comorbidities such as hypertension and dyslipidemia, the adoption of healthy lifestyle changes, and a plan that includes the patient in all aspects of care is more likely to achieve the desired results, with more favorable outcomes for both mother and child.

Diabetes Care Before and During Pregnancy



What kind of diabetes care is needed for these women? Type 1 and type 2 preexisting diabetes require preconception planning. Women who have had a previous pregnancy complicated by gestational diabetes also require preconception planning for future pregnancies.

Pregnancy is not recommended when certain medical conditions are present. For instance, a woman with ischemic heart disease may be cautioned against pregnancy. Both the American Diabetes Association and the American Association of Diabetes Educators recommend a full discussion of all potential risks during any preconception counseling session.

Some diabetes-related complications like retinopathy and nephropathy can worsen during pregnancy and a complete discussion with the patient about these issues is recommended.

Gestational diabetes care should include a risk assessment, screening guidelines, and follow-up care. The American Diabetes Association recommends that risk assessment be undertaken at the first prenatal visit and that women with high risk factors undergo glucose testing.

Women with preexisting or gestational diabetes should be informed about the options for management of the condition, monitoring of blood glucose, symptoms of hyperglycemia and hypoglycemia, care during labor, delivery and postpartum, and possible fetal complications.

Check Point

Infant mortality rates due to diabetes have declined since the 1960s in part because:

- a) fewer babies are being born
- b) better glycemic control has led to improved outcomes
- c) technology has made care more complicated
- d) patients are leaving their care completely in the hands of their healthcare professionals

Let us take this opportunity to test your understanding of the material we have covered so far. Infant mortality rates due to diabetes have declined since the 1960s in part because:

- a) fewer babies are being born
- b) better glycemic control has led to improved outcomes
- c) technology has made care more complicated or
- d) patients are leaving their care completely in the hands of their healthcare professionals.

The answer is (b).

Infant mortality rates due to diabetes have declined since the 1960s in part because better glycemic control has led to improved outcomes.

If you answered b you are correct. Infant mortality rates due to diabetes have declined since the 1960s in part because better glycemic control has led to improved outcomes.

Preexisting Diabetes

Let us take a closer look at preexisting diabetes and how it impacts pregnancy.

Preconception Planning

- Assessment of general health
- Discussion of benefits of prepregnancy planning and of risks for compromised maternal health
- Obstetric evaluation
- Optimal diabetes control
- Contraception counseling
- Education of the woman and family

We know that two thirds of pregnancies in women with type 1 or type 2 diabetes are unplanned. The American Diabetes Association suggests that preconception counseling should ideally begin at the onset of puberty and continue through to menopause. Preconception care should begin at least 3–6 months prior to conception because many birth defects manifest during the first trimester. For women who develop gestational diabetes, preconception counseling should start immediately following delivery to prepare for the next pregnancy.

Poorly controlled diabetes during the early weeks of pregnancy significantly increases the risk of first trimester spontaneous abortions or of delivering an infant with a major anomaly.

Elements of preconception counseling usually include a discussion of the benefits of prepregnancy planning, discussion of physiological and psychological readiness for pregnancy and possible risks, identification of any diabetes-related complications, and referral for an obstetric evaluation. Regardless of how long the person has had diabetes, a thorough assessment of self-management skills including blood glucose monitoring, insulin injection technique, and nutrition should be conducted. Nutritional information should focus on meal planning and the need to increase protein and certain vitamins necessary for a healthy pregnancy. It should also include a discussion regarding contraception, the importance of good glycemic control prior to discontinuation of contraception, and inclusion of the woman and her family in the education process.

Preconception Assessment

- History & Physical
- Laboratory evaluation
 - A1C
 - UA & Culture
 - 24-hr urine for creatinine clearance/protein/microalbumin
 - Thyroid panel
- Special studies (if indicated)
 - EKG
 - Testing for neuropathy
 - Retinal exam

A preconception assessment of a woman with preexisting diabetes should start with a detailed medical history and physical examination that includes the type of diabetes, age of onset, duration and course of disease, history of acute and chronic complications, current regimen with attention to routine insulin dosages (if applicable), diet, exercise, hypoglycemia unawareness, self-monitoring of blood glucose, and a review of other medical problems, taking special note of hypertension and dyslipidemia. Also included is any obstetrical history with particular attention to infertility problems and pregnancy complications, notation of all medications, and the identification of the woman's support system including her family and work environment.

Laboratory evaluations should include a hemoglobin A1C to evaluate recent glycemic control, urinalysis and culture to rule out any urinary tract infection, a 24-hr urine for creatinine clearance/total protein/microalbumin to assess renal function, a thyroid panel, and blood lipids levels. Other special studies may be indicated to assess severity if complications are present or are identified by the laboratory test results. These tests may include an electrocardiogram, neuropathic testing, and a retinal exam.

Possible Contraindications

- ❑ Pregnancy is not recommended when certain diabetes-related complications are present
 - Ischemic heart disease
 - Active proliferative retinopathy
 - Renal insufficiency
 - ❑ Serum creatinine >2 mg/dL
 - ❑ Blood pressure >130/80 mm Hg despite treatment
 - Severe gastroenteropathy

If a woman is found to have ischemic cardiac disease, the risks of maternal mortality are high, and the woman with very serious complications may need to be counseled against becoming pregnant.

If significant proliferative retinopathy is present, the woman may be advised to delay the pregnancy until treatment can stabilize the condition. Background retinopathy that occurs during pregnancy usually regresses after delivery.

If significant renal disease is present, the woman must be warned about the high risk of infant morbidity and mortality associated with this particular complication. Renal disease can be validated by a serum creatinine of over 2 mg/dL and/or a creatinine clearance of less than 50 ml/min. Significant proteinuria of more than 2 grams in 24 hours, when accompanied by hypertension, indicates a significant risk to mother and child.

When blood pressure is between 130/80 and 140/90, therapeutic lifestyle changes are usually recommended, while hypertension treatment is initiated when blood pressure is over 140/90.

During pregnancy and in the presence of renal insufficiency, it is recommended that blood pressure be maintained at less than 130/80. The use of an angiotensin converting enzyme or ACE inhibitor should be discontinued and be replaced with other antihypertensive medications since ACE inhibitors may cause anomalies of the genitourinary tract in the fetus.

If the woman has severe gastroenteropathy, the physician may consider this a relative contraindication to pregnancy. Gastroenteropathy results in poor absorption and metabolic control for both the woman and her developing baby. Therefore, glucose homeostasis is very difficult to maintain.

Possible Maternal Complications

- Hypertension
 - Preeclampsia/Eclampsia
- Polyhydramnios
- Genitourinary infections
- Premature labor
- Increased rate of C-section delivery

In addition to an increased risk of hypoglycemia and ketoacidosis during pregnancy, the risk for developing the most common maternal complications is increased by diabetes. These maternal complications including pregnancy-associated hypertension, chronic hypertension, and preeclampsia/eclampsia, are a leading cause of fetal and maternal morbidity and mortality. Hypertensive complications occur in 5%–10% of all pregnancies.

Preeclampsia, sometimes called toxemia of pregnancy, is hypertension with proteinuria or edema. This can develop between week 20 and the end of the pregnancy. Eclampsia is a more severe form that can result in seizures and coma.

Polyhydramnios or an excessive amount of amniotic fluid is also a risk that may promote premature labor.

Urinary tract infections occur in 4%-10% of pregnant women. These include bacterial infections of the genitourinary tract, cystitis of the bladder, and pyelonephritis in the kidneys. Diabetes increases the risk of urinary tract infections by 2- to 4-fold, as well as the risk for vaginal infections, premature labor, and the need for cesarean delivery.

Gestational Diabetes

Now let us focus our attention more closely on gestational diabetes and the special concerns and management needed for a successful outcome.

Risk Factors for GDM

Risk Factors Include:

- Family history of diabetes
- Obesity (BMI >30)
- Age >25 years
- History of abnormal glucose metabolism
- History of poor obstetric outcome or previous GDM
- High-risk ethnic group
- Polycystic ovary syndrome

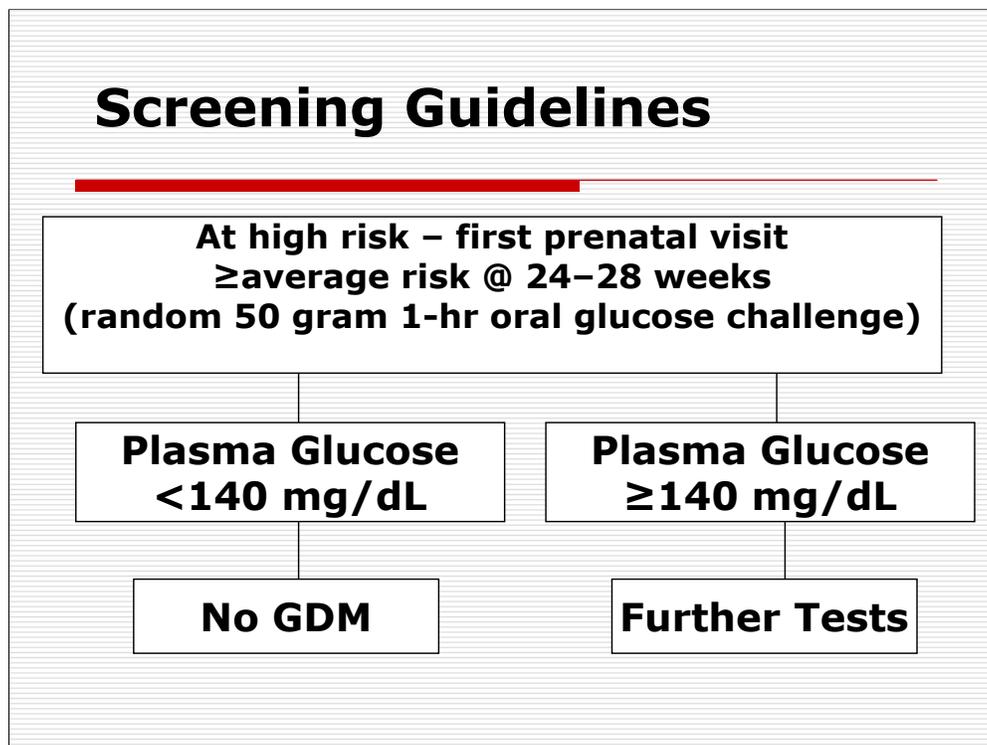
The risk factors for gestational diabetes include a strong family history of diabetes in parents or siblings; obesity, with a body mass index over 30; maternal age over 25; or a prior history of abnormal glucose metabolism including a fasting plasma glucose over 126 mg/dL. A fasting plasma glucose of over 126 mg/dL warrants immediate evaluation.

In addition to a history of poor obstetric outcomes or a previous history of gestational diabetes, being a member of certain ethnic groups increases risk. These high risk groups include African Americans, Native American Indians, Hispanics/Latinos, Asian Pacific Islanders/Southeast Asians, Asian Indians, and indigenous Australians.

A recent article, published in the *Journal of the American Medical Association*, reported that a woman's own birth weight was inversely related to her risk of gestational diabetes, suggesting that early life factors may be important in the etiology of this disorder.

In addition, polycystic ovary syndrome, with its relationship to insulin resistance, is common in women with type 2 and gestational diabetes.

Screening Guidelines



In its 2004 clinical practice recommendations, the American Diabetes Association suggests that a risk assessment be conducted at the first prenatal visit to evaluate patients at high risk for developing gestational diabetes.

Screening should be done between the 24th and 28th weeks of gestation for all pregnant women, with glucose testing performed on women with average or above average risk, including any woman over age 25. Women considered low risk do not require glucose testing.

Screening can be a random 50 gram 1-hour oral glucose challenge that can be administered without regard for time of day or the time interval since the last meal.

If the plasma glucose is less than 140 mg/dL there is no gestational diabetes. However, the provider may repeat the test again later in the pregnancy for high-risk individuals.

If the plasma glucose result is 140 mg/dL or greater, further testing is required.

Screening Guidelines

**At 24–28 weeks gestation
(random 50 gram 1-hr oral glucose challenge)**

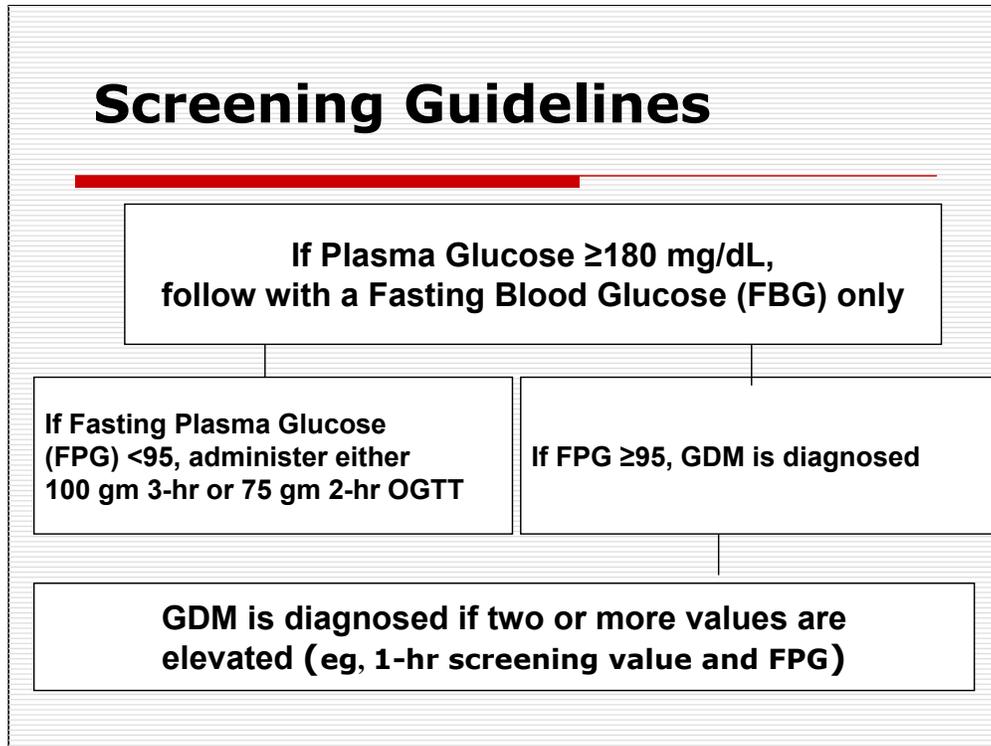
If plasma glucose ≥ 140 – < 180 mg/dL

**Administer 100 gram 3-hr
oral glucose tolerance test**

If the 50 gram 1-hr oral glucose challenge screening value is greater than or equal to 140 mg/dL, but less than 180 mg/dL, gestational diabetes may be present.

To confirm the diagnosis, a 100 gram 3-hr oral glucose tolerance test (OGTT) is administered after an overnight fast, preferably within one week. This test will identify 80% of those with gestational diabetes.

Screening Guidelines



Screening guidelines recommend that if the value for fasting plasma blood glucose is 180 mg/dL or higher, a second test should be scheduled immediately to confirm the diagnosis.

Gestational diabetes is diagnosed when two or more of the plasma glucose values meet or exceed the diagnostic criteria:

- Fasting level greater than or equal to 95 mg/dL
- 1-hour result greater than or equal to 180 mg/dL
- 2-hour result greater than or equal to 155 mg/dL
- 3-hour result greater than or equal to 140 mg/dL
- If the fasting plasma glucose is less than 95, it is safe to continue with the full 2- or 3-hr OGTT.

If results reveal only one abnormal value, patients may be managed with an individual meal plan and exercise program, and retested at 32–34 weeks gestation.

Check Point

A woman is considered at high risk for gestational diabetes if she:

- a) is obese
- b) has a history of abnormal glucose metabolism
- c) belongs to a high risk ethnic group
- d) all of the above

Let us see what you recall about an important point made thus far.

A woman is considered at high risk for gestational diabetes if she:

- a) is obese
- b) has a history of abnormal glucose metabolism
- c) belongs to a high risk ethnic group or
- d) all of the above.

The answer is (d).

A woman is considered at high risk for gestational diabetes if she is obese, has a history of abnormal glucose metabolism, or belongs to a high risk ethnic group.

If you answered d, you are correct. A woman is considered at high risk for gestational diabetes if she is obese, has a history of abnormal glucose metabolism, or if she belongs to a high risk ethnic group.

Metabolic Demands of Pregnancy

Preexisting and GDM

Let us move on and we'll continue our review with a discussion about the metabolic demands of both preexisting and gestational diabetes.

Changes in Metabolism During Pregnancy

Provision of glucose to fetus results in

- Decreased fasting maternal glucose levels
- Increased plasma ketones
- Lower concentrations of most amino acids
- Increased insulin levels

Hormones increased during pregnancy

- Human Placental Lactogen (HPL)
- Estrogen
- Progesterone
- Cortisol
- Prolactin

There are a myriad of changes in metabolism during pregnancy.

First there is a provision of glucose and gluconeogenic substrate to the fetus that results in a drop in maternal glucose levels to 55–65 mg/dL in the fasting state, well below nonpregnant fasting glycemia. Simultaneously, plasma ketone concentrations are higher than usual, and free fatty acid levels are elevated after an overnight fast. Thus, pregnancy simulates a state of “accelerated starvation,” leading to the increased use of alternate fuels for maternal metabolism while glucose is spared for fetal consumption.

Amino acids are actively transported to the fetal circulation, resulting in lower circulating concentrations of most amino acids.

Circulating insulin levels are increased, especially in late pregnancy, in part because of accelerated hormonal activity counteracting insulin action. The hormones that are increased in late pregnancy include: human placental lactogen, estrogen, progesterone, cortisol, and prolactin.

Changes in Metabolism During Pregnancy

- Food ingestion results in higher and more prolonged plasma glucose concentration
 - Enhances transplacental delivery of glucose to the fetus and promotes growth of the fetus
- Maternal insulin and glucagon do not cross the placenta

The fed state is also modified in pregnant women with food ingestion resulting in higher and more prolonged plasma glucose concentration. This more sustained postprandial hyperglycemia enhances transplacental delivery of glucose to the fetus and promotes growth of the fetus. But it is important to note that maternal insulin and glucagon do not cross the placental barrier.

Management Issues

Preexisting and GDM

Next, we will take a closer look at the management issues with preexisting and gestational diabetes before, during, and after pregnancy.

Recommended Medical Management

- Patient/healthcare provider team
- Develop a treatment plan
- Provide education and encourage self-monitoring of blood glucose (SMBG)
- Monitor maternal and fetal well-being
- Control glucose during labor and delivery
- Control glucose levels during postpartum period

The following points are the recommended goals and guidelines that should be part of a comprehensive diabetes management program for pregnant women.

Foremost, patients and healthcare providers should work as a team to determine management strategy. It should include preconception and postpartum care as well as the care during pregnancy. A treatment plan that includes nutrition, exercise, and medications should be developed. The plan should encourage glucose monitoring multiple times daily for confirmation of glycemic control. Ongoing counseling and resources for diabetes education should be available to the woman and her family.

Monitoring of maternal and fetal well-being should be continuous through the labor, delivery, and postpartum period due to the high risk of complications. It is critical for both the mother and the child to be monitored (and for glucose to be controlled) during labor and delivery, and during postpartum recovery.

Glycemic Goals in Pregnancy

Plasma Blood Glucose*

<input type="checkbox"/> <u>Fasting/Premeals</u>	<u>65–100</u> mg/dL
<input type="checkbox"/> <u>1 hr postprandial</u>	<u>110–135</u> mg/dL
<input type="checkbox"/> <u>2 hr postprandial</u>	<u><120</u> mg/dL
<input type="checkbox"/> <u>2 am – 6 am</u>	<u>65–135</u> mg/dL

*These values are about 10% lower in whole blood.

In pregnant women without diabetes, maternal plasma glucose remains in the 100 mg/dL range with fasting levels of 60 mg/dL and postprandial levels of 120 mg/dL.

The American Diabetes Association recommends the following therapeutic blood glucose targets for pregnancies complicated by diabetes:

- A fasting/premeal plasma value of 65–100 or whole blood values of 60–90 mg/dL
- A 1-hr postprandial plasma value of 110–135 or whole blood values of 100–120 mg/dL
- A 2-hr postprandial plasma value of less than 120 or whole blood values of less than 110 mg/dL
- When middle-of-the-night testing is needed, plasma values should be between 65 and 135 mg/dL or whole blood values between 60 and 120 mg/dL

Ideally, premeal, postprandial and bedtime blood glucose testing is recommended. This is especially necessary for those women on multiple daily insulin injections or those being managed with continuous subcutaneous insulin infusion or insulin pump therapy. Middle-of-the-night testing is also recommended if there is any suspicion of nighttime hypoglycemia. Daily testing schedules need to be individualized but generally involve testing as many as 6-8 times a day.

Patient Management Guidelines

- Nutritional management
- Regular physical activity program
- Administration of insulin when necessary with appropriate adjustment of doses
- Self-monitoring of blood glucose and ketones
- Treatment of hypoglycemia
- Techniques to enhance coping skills

The American Diabetes Association recommends a management plan that includes education about the same skills required for any insulin-based self-management program. This includes nutritional management, a plan for regular physical activity, administration of insulin with appropriate adjustment of doses to maintain glucose results within goals, self-monitoring of blood glucose and ketone testing, including documentation, and more importantly education in the interpretation of the results.

Ketone monitoring can be useful for detection of insufficient carbohydrate and calorie intake, or metabolic changes caused by illness, infection, or stress. Blood testing is preferred as urine results may not reflect the current clinical situation. It is recommended that blood ketones be checked whenever there is any unexplained blood glucose level >300 mg/dL.

The management plan should also include a review of the proper treatment of hypoglycemia, including the use of glucagon, and the techniques to enhance coping skills.

Medical Nutrition Therapy

- Individual dietary consult
- Additional protein
- Additional calcium, iron, folate
- Dietary composition should be individualized

The American Diabetes Association recommends that women receive nutritional counseling by a registered dietitian. This counseling should include individualized medical nutrition therapy recommendations where appropriate. For example, the dietitian may recommend that an obese women limit daily calories to 25 kcal/kg to avoid ketonemia. Self blood glucose monitoring and other metabolic measures can be used to monitor the effectiveness of the nutrition therapy plan.

Complex carbohydrates, monounsaturated and polyunsaturated fats, and foods high in fiber should be encouraged. Additional protein, calcium, iron, and folate are recommended to support fetal growth and increased maternal metabolic demand.

A 1-hr postprandial glucose test of less than 120 mg/dL is positively related to the neonatal birth weight in pregnancies complicated by diabetes and should be your target.

Physical Activity

- Physician clearance
- Physical activity
 - Cardiovascular, strength, flexibility
- Identification of appropriate exercises
 - Individualized program with realistic goals
 - Certain exercises contraindicated during pregnancy (eg, supine after 1st trimester)
- Education regarding monitoring well-being during activity
- Explanation of risks and contraindications

Exercise activities can be broadly divided into cardiovascular or aerobic, resistance or strength, and stretching for flexibility. In the absence of contraindications, a pregnant woman can maintain a moderate activity level. However, a physician's clearance is recommended.

Discussion with a professional is recommended for identification of appropriate exercises and the development of an individualized program with realistic goals. Certain exercises, such as those requiring a supine position after the first trimester, are not appropriate because they may place stress on the fetus by limiting oxygen flow.

Education of patients regarding monitoring of their well-being during activity is recommended. Individuals can be taught to monitor breathing, using the talk test. Can they talk comfortably during the exercise? Also monitoring of maternal heart rate, temperature, and muscle fatigue are good measures of well being.

Insulin Therapy

- ❑ Early pregnancy: insulin requirements diminish
- ❑ 2nd, 3rd trimesters: insulin requirements gradually increase 2-fold
- ❑ In GDM: insulin recommended when fasting glucose level is >105 mg/dL
- ❑ When properly dosed, insulin is the most effective and safest therapy for lowering blood glucose
- ❑ Women with type 2 diabetes may discontinue oral antidiabetic therapy (OAD); most OADs are not recommended during pregnancy

In preexisting diabetes, insulin requirements diminish in early pregnancy because of decreased maternal glucose concentration as the needs of the fetus for glucose increase. But in the second and third trimesters, insulin requirements gradually increase because of the increased placental production of the “contra-insulin” hormones of pregnancy namely, lactogen, prolactin, estrogen, and progesterone. These hormones may increase to as much as twice usual levels.

In gestational diabetes, insulin is recommended when the fasting plasma glucose level is more than 105 mg/dL or postprandial plasma glucose is over 155 mg/dL at 1 hour, or over 130 mg/dL at 2 hours. Some healthcare providers may aim for lower fasting plasma glucose and postprandial values in patients with gestational diabetes requiring insulin. When properly dosed, insulin is the most effective and safest therapy for lowering blood glucose and it has been consistently shown to reduce fetal morbidities.

Clinicians may recommend that women with type 2 diabetes discontinue oral anti-diabetic agents, as many of these agents cross the placenta and may increase fetal insulin production. If the pregnancy is planned, the patient can begin insulin therapy before conception.

Most oral anti-diabetic agents are pregnancy category C drugs and are not recommended during pregnancy or lactation, nor are they FDA approved for use in gestational diabetes. Several clinical studies have suggested that the second-generation sulfonylurea, glyburide, can be effective and safe in some patients with GDM because it does not cross the placenta. Both glyburide and metformin are considered pregnancy category B drugs. Further randomized trials are needed to verify the efficacy and safety of these oral anti-diabetic agents during pregnancy.

Insulin Therapy (cont)

- ❑ SMBG is used to determine amount of insulin required and timing of doses
- ❑ Basal, prandial, and bedtime doses can be adjusted as necessary
- ❑ Use of a rapid-acting insulin analog can lower postprandial glucose (PPG) more effectively than regular insulin
- ❑ Insulin pumps are well tolerated in women with GDM or type 2 diabetes who need large amounts of insulin

Self-monitoring of blood glucose is used to determine the amount of insulin required, the timing of doses, as well as the effects of food and exercise. Basal, prandial, and bedtime insulin doses can be adjusted as necessary based on these results. No published guidelines have been issued as to how often to test and the clinician should consider the patient's preferences and ability to cope with monitoring an insulin therapy regimen.

A recent article in *Diabetes Care* suggested that a rapid-acting insulin analog, insulin aspart, is more effective than regular insulin for lowering postprandial glucose levels and reducing the overall glucose exposure for the developing fetus. However, further studies of insulin analogs in gestational diabetes are required. Elevated PPG levels have been associated with an increased risk of macrosomia. Macrosomia is discussed later in the program.

A study comparing the use of insulin pump therapy to multiple daily injections in women with type 1 diabetes found that achieving good metabolic control was the critical factor in avoiding risk of fetal malformation, regardless of whether multiple daily injections or continuous subcutaneous insulin infusions were used. Also of interest is a study from 2001 that found in women with gestational or type 2 diabetes, the use of a pump was well tolerated, especially in those taking large amounts of insulin; however, use of a pump was also associated with an increased weight gain.

Insulin Therapy (cont)

- ❑ Specific insulin formulations are prescribed based on fasting and postprandial blood glucose
- ❑ If only PPG is abnormal, rapid-acting insulin may suffice
- ❑ If FPG is also elevated, intermediate- or long-acting insulin may also be required
- ❑ Twice-daily or intensive therapy may be needed

The decision about the type and amount of specific insulin formulations that are prescribed should be based on fasting and postprandial blood glucose. If only the postprandial glucose is abnormal, a rapid-acting insulin pre-meal may suffice. However, if the fasting plasma glucose is also elevated, an intermediate- or long-acting insulin may also be required. Twice-daily regimens, such as a mixture of rapid- or short-acting, with intermediate acting insulin or a more intensive insulin therapy regimen, may be used.

Monitoring Glycemic Control

- Self-monitoring of blood glucose (SMBG) at least 4 times daily if on insulin
- Women with GDM not on insulin measure fasting and 1-hr postprandial BG
- A1C measured quarterly
- Ketone monitoring is recommended throughout pregnancy (ketones cross the placenta)

Maintaining close-to-normal blood glucose levels is essential to avoiding complications. Experts recommend self-monitoring of blood glucose at least 4 times daily for women on an insulin regimen with at least one postprandial measurement. Women not on insulin should check blood glucose in the morning and 1-hr postprandial after each meal. Peak postprandial response has been the best predictor of the risk of macrosomia.

A hemoglobin A1C should be measured at least quarterly and again ketone monitoring is recommended throughout pregnancy as ketones cross the placenta, and there is some evidence that the ketones may be harmful to the fetus.

Barriers to Successful Outcomes

- Fear of physiological changes, worsening of diabetes, not producing a healthy baby
- Absence of emotional support
- Lack of psychosocial assessment/ counseling

Many factors can present as barriers to adherence to diabetes management programs. All women go through adjustment stages during their pregnancy, and these are magnified in women with diabetes by the need to have better glycemic control during pregnancy. Increased anxiety about the effects of diabetes on herself and on the fetus, and doubts about her ability to manage both pregnancy and diabetes may play a role in willingness to undertake the added responsibility of close adherence to a demanding treatment plan.

The intensity of following a strict protocol “emotionally lengthens” the pregnancy time span for even the most cooperative patient. Emotional support is an essential part of well-being from whatever the source: spouse, other family members, healthcare professionals, peers, or support groups. Open communication between the patient and her team members requires mutual respect, honesty, and cooperation.

A psychosocial assessment can provide valuable information about lifestyle, family, job, and economic situation, as well as assist in providing advice that can improve adherence to the treatment plan leading to a more positive outcome.

Predictors of Poor Outcomes

- Poor maternal glucose control
 - Ketoacidosis, associated intrauterine deaths, birth anomalies are most common in those with poor blood glucose control
- Vascular disease
 - Hypertension
 - Preeclampsia
- Microvascular disease
 - Patients with nephropathy are at increased risk

Metabolic control is an important predictor of a poor pregnancy outcome. Ketoacidosis and associated intrauterine deaths, as well as birth anomalies, are most common in those with poor blood glucose control. Vascular complications, especially hypertension and preeclampsia, may also influence the outcome. The greater the degree of hypertension, the greater the likelihood of a poor outcome for mother and child.

Those patients with nephropathy are at increased risk for preeclampsia, fetal-growth restriction, and preterm delivery, and they have a 3-fold increase in the rate of stillbirth over women who have diabetes but who do not have nephropathy.

Congenital Anomalies Fetal Monitoring Complications

Preexisting and GDM

What types of congenital anomalies can be expected? How can fetal monitoring help? Let us take a look now at the complications of the fetus in preexisting and gestational diabetes.

Possible Congenital Malformations

<u>Anomaly</u>	<u>Ratio of incidence*</u>
<input type="checkbox"/> Caudal regression	252
<input type="checkbox"/> Situs inversus	84
<input type="checkbox"/> Renal anomalies (total)	38
<input type="checkbox"/> Heart anomalies	4
<input type="checkbox"/> Anencephalus	3
<input type="checkbox"/> Anal/rectal atresia	3
<input type="checkbox"/> Spina bifida or other CNS	2

*Ratio of incidence is in comparison to the general population

This table gives you some indication of the incidence of congenital malformations for those with a diabetes complicated pregnancy versus women with a nondiabetes complicated pregnancy. The highest anomaly is caudal regression (lower spinal defects) with a ratio of incidence of 252 compared to the nondiabetes complicated pregnancy. This is followed by situs inversus (reversal of positions of internal organs, which rarely causes symptoms or complications) with an incidence of 84, and renal anomalies at 38. In addition, there is an increased incidence of spina bifida and other central nervous system anomalies such as anencephalus, cardiac anomalies, and anal/rectal atresia.

Monitoring Fetal Status

Test	Purpose	Timing (wk)	Comment
Ultrasound	Screen for structural anomalies	After 7.5	Detects major anomalies only
α -fetoprotein	Screen for open fetal defect	16	Detects neural tube defects
Amniocentesis	Lung maturity Genetic abnormality	16	High false-positive rate

The testing to monitor fetal well being during the pregnancy is done at the discretion of the physician and is based on individual needs.

Ultrasound testing is most commonly performed during the first trimester to estimate date of delivery and during the second trimester to identify structural abnormalities. It may be indicated during the third trimester to assess fetal growth and development and may be done as needed to measure amniotic fluid levels.

In early pregnancy, ultrasound can show the presence of malformations such as neural tube defects. In addition, serial ultrasounds can demonstrate growth patterns that can assist in identifying large or small infants for gestational age.

Alpha-fetoprotein is a maternal blood test that can identify a fetus at risk for neural tube defects which has a 10–20 times greater risk in diabetes complicated pregnancies than those of the general population.

Amniocentesis assesses fetal lung maturity and genetic markers of birth defects. This test is routinely performed during the late first trimester for women over 35 years of age to diagnose chromosomal abnormalities, although there have been reports of a high false-positive rate in this group.

Monitoring Fetal Status

Test	Purpose	Timing (wk)	Comment
Nonstress	Screen for fetal well-being	35–40	May result in false positives
Biophysical	Evaluate fetal problems	35–40	Reliable profile
Fetal activity	Screen for fetal well-being	32–40	Simple, inexpensive

A reactive nonstress test evaluates the absence or presence of fetal compromise. A nonreactive nonstress test may be seen in sleep states or other conditions that are not necessarily adverse.

A biophysical profile, which is a combination of a nonstress test and an ultrasound evaluation, may be done if the nonstress test results are questionable. These tests may be done biweekly, weekly, or daily depending on individual circumstances.

Fetal activity is a simple, inexpensive method of monitoring fetal well-being. Beginning at 30–32 weeks of gestation several protocols, for example, kick counting, can be taught to the mother. The patient is instructed to measure and record perceived fetal movements in a given time period and notify the healthcare provider if there is a change.

Possible Fetal/Neonatal Short-Term Complications Linked to Uncontrolled Diabetes

- Hypoglycemia
- Hypocalcemia
- Hypomagnesemia

Several short term fetal and neonatal complications related to a pregnancy complicated by uncontrolled diabetes can be prevented or reduced if the patient can establish and maintain near normal blood glucose levels before and during pregnancy. Neonatal hypoglycemia in the newborn, defined as a glucose level less than 35 mg/dL for both term and preterm infants, is the most common neonatal metabolic complication. It is seen in 10%–25% of all infants born to mothers with diabetes.

If maternal diabetes is poorly controlled, the fetus receives more glucose and alternate fuel sources than it requires for normal growth, and must secrete additional amounts of insulin to use this excess glucose. At delivery, the glucose supply decreases but the baby continues to secrete the high amounts of insulin, which can result in neonatal hypoglycemia. This is usually treated by early feeding and IV glucose if necessary.

Hypocalcemia affects about 50% of newborns and hypomagnesemia about 33%. These neonatal complications should be promptly diagnosed and treated. They are probably related to the severity of maternal diabetes which can cause a secondary transient hypoparathyroidism during the first 2–4 days of life. Hypomagnesemia may be the result of blunted secretion of parathyroid hormone; hypocalcemia may be secondary to hypomagnesemia.

Possible Fetal/Neonatal Short-Term Complications Linked to Uncontrolled Diabetes (cont)

- Hyperinsulinemia
- Polycythemia
- Cardiomyopathy
- Hyperbilirubinemia
- Stillbirth and respiratory distress syndrome

Continuing fetal hyperinsulinemia decreases hepatic glucose production and blunts the rise of counterregulatory hormones (human placental lactogen, estrogen, progesterone, and cortisol), which can further promote neonatal hypoglycemia.

Polycythemia (high red blood cell levels) is associated with increased levels of erythropoietin. Venous hematocrits, over 65%–70%, have been observed in 20%–40% of newborns during the first days of life. Polycythemia is probably secondary to chronic intrauterine hypoxia caused by hyperglycemia and hyperinsulinemia. The anabolic effect of hyperinsulinemia can also lead to cardiomyopathy.

The cause of hyperbilirubinemia is multifaceted. Potential causes include increased hemolysis and ineffective erythropoiesis, increased bruising and trauma, and/or a delay in liver enzyme maturation.

Stillbirth and respiratory distress syndrome are now less common, due to sophisticated monitoring techniques, prolongation of pregnancy beyond 38 weeks gestation, and demonstrated evidence that glycemic control is critical.

Fetal Macrosomia

- ❑ Major complication of GDM
- ❑ Birth weight >4,000 g
- ❑ Increasing in the United States
- ❑ Mainly affects heart, liver, and subcutaneous fat
- ❑ Potential complications for infant
 - Shoulder dystocia, fractured clavicles, brachial plexus injury, asphyxia
- ❑ Can lead to adolescent obesity and type 2 diabetes

Macrosomia is one of the most common complications of gestational diabetes. Macrosomia is typically defined as a fetus weighing more than 4,000 grams; although definitions do vary among professional societies.

Fetal hyperinsulinemia is caused by increased maternal-fetal transfer of glucose and other nutrients that increase fetal growth during late gestation. Insulin is the primary growth factor during this period and increases body fat results.

The incidence of macrosomia is increasing in the United States, possibly because of rising rates of obesity and diabetes. It occurs in 10% of all pregnancies in the general population, but with diabetes, the incidence increases to between 20% and 32%, according to the American Association of Diabetes Educators.

Macrosomia mainly affects fetal heart, liver, and subcutaneous fat. It increases the demand for oxygen and asphyxia may result, which is associated with difficult labor and delivery.

The potential complications related to macrosomia for the infant include shoulder dystocia, fractured clavicles, brachial plexus injury, and asphyxia. Macrosomia has also been found to lead to adolescent obesity and type 2 diabetes.

Check Point

Possible fetal complications related to uncontrolled diabetes include:

- a) hypocalcemia
- b) macrosomia
- c) cardiomyopathy
- d) all of the above

We are at another checkpoint. Let us see what you recall.

Possible fetal complications related to uncontrolled diabetes include:

- a) hypocalcemia
- b) macrosomia
- c) cardiomyopathy, or
- d) all of the above.

The answer is (d).

Possible fetal complications related to uncontrolled diabetes include, hypocalcemia, macrosomia, or cardiomyopathy.

Did you answer d? Great! Possible fetal complications related to uncontrolled diabetes include all three complications- hypocalcemia, macrosomia, and cardiomyopathy.

Management of Labor and Delivery

Postpartum Care and Follow-up

Preexisting and GDM

Let us move forward in the pregnancy and take a closer look at the management of labor and delivery, the postpartum period, and follow-up care.

Management of Labor and Delivery

- Continuous fetal heart rate monitoring
- Maintain maternal plasma glucose levels between 70–100 mg/dL
- Continuous infusion of both insulin and glucose as required
- Maternal bedside glucose monitoring (hourly and as needed)

Management during labor and delivery should include continuously monitored fetal heart rate. Maternal blood glucose levels should be measured hourly with the goal to maintain levels between 70–100 mg/dL.

Patients with preexisting diabetes may be placed on an IV insulin drip during labor to more easily manipulate the insulin dose. There are numerous intrapartum insulin management protocols recommending the initiation of IV insulin therapy at blood glucose levels ranging from 90 to 140 mg/dL. A useful protocol is:

- If the plasma blood glucose value is between 100–150 mg/dL, add insulin to IV of normal saline solution and administer at the rate of 1 unit per hour.
- If the plasma blood glucose value is over 150 mg/dL, insulin is infused at the rate of 2 units per hour.
- If blood glucose remains over 100 mg/dL for 2 hours after initiation of insulin, the rate is increased by 0.5 unit per hour; repeat every 2 hours if blood glucose remains elevated.
- Insulin is discontinued when blood glucose levels fall below 100 mg/dL.
- If a blood glucose level falls below 70 mg/dL, the infusion solution is changed to a 5% dextrose solution.
- Women with uncontrolled diabetes may need from 0.5 to 2.5 units of insulin per hour during active labor.

Women with gestational diabetes usually do not require any insulin during labor; however the same protocol can be used if blood glucose values are not between 70–100 mg/dL.

After Delivery

- Insulin requirements are usually significantly lower
- Breastfeeding is recommended
- Women with type 2 diabetes may continue with insulin therapy during lactation

Following delivery, insulin requirements are usually significantly lower. Euglycemia remains the goal. If blood glucose levels do not return to normal, there may be an underlying infection.

Women with gestational diabetes usually do not need further insulin and women with preexisting diabetes may need no insulin for 24–48 hours after delivery and should be monitored carefully.

Breastfeeding is recommended. Breastfeeding mothers may require less insulin because of the greater amount of calories expended when nursing. In general, insulin requirements are recalculated at 0.6 units per kilogram of their current weight for nonlactating women and 0.4 units per kilogram of their current weight for lactating women. Nutritional requirements for a women with preexisting diabetes should focus on maintaining blood glucose control and meeting the nutritional needs of lactation. The same meal plan as that of the third trimester is usually appropriate during lactation. The addition of a bedtime snack may be needed. Women with type 2 diabetes whose glucose value cannot be maintained through meal planning alone may need to continue to inject insulin while breastfeeding since oral glucose-lowering agents cannot be used during lactation.

Postpartum GDM Follow-up

- ❑ 75 gram 2-hr OGTT at 6–8 week check or after lactation for reclassification of diabetes
- ❑ If normal, annual FBG as follow-up
- ❑ Preconception counseling prior to next pregnancy
- ❑ Growth and development of child should be monitored

Postpartum follow-up for women who had gestational diabetes should include the continuation of blood glucose testing during the postpartum period to assess for the existence of previously undiagnosed type 2 diabetes.

The recommended testing is a 2-hr, 75 gram oral glucose tolerance test performed at the 6–8 week postpartum visit, or after lactation. If the results are within the normal range, then it is recommended that annual testing be done thereafter.

Normoglycemia is defined as fasting plasma glucose values of less than 100 mg/dL or a 2-hr plasma value of less than 140 mg/dL. Abnormal oral glucose tolerance test values are classified into two categories: impaired glucose tolerance or type 2 diabetes.

Diabetes is diagnosed if the fasting plasma glucose value is greater than or equal to 126 mg/dL, or if the 2-hr plasma value is greater than or equal to 200 mg/dL as measured on 2 separate occasions. Impaired fasting glucose is defined as a fasting result between 100–125 mg/dL.

Women who test positive for diabetes or impaired glucose tolerance should be referred to a healthcare provider familiar with the treatment and management of diabetes. Patients who are not diagnosed with type 2 diabetes should be advised of their increased risk for developing gestational diabetes with subsequent pregnancies, as well as for developing type 2 diabetes later in life.

Screening and preconception counseling should be planned before the next pregnancy is considered. Remind mothers that infants of mothers with diabetes have an increased risk of obesity and glucose intolerance in adolescence so that growth and development of the child should be monitored carefully.

Future Risks for GDM Patients

A woman who has had gestational diabetes is at significant risk to develop:

- GDM in subsequent pregnancies – 60%–70% risk
- Risk for future type 2 diabetes
 - 40%–60% risk within 5–15 years
 - If obese, 50%–75% risk
 - If FBG with OGTT \geq 130 mg/dL - 95% risk
 - Predictors of prediabetes or type 2 diabetes
 - Maternal obesity
 - Elevated FBG on OGTT
 - GDM diagnosed early in gestation

Women who have had gestational diabetes are at risk for developing type 2 diabetes in the future. Those who have had gestational diabetes have a 60%–70% chance of developing gestational diabetes with subsequent pregnancies and they are at a 40%–60% increased risk of developing type 2 diabetes compared to the general population, usually within 5–15 years. A plasma glucose value of more than or equal to 130 mg/dL on the 75-gram oral glucose tolerance test, increases the risk of developing type 2 diabetes to 95%.

An appropriate meal plan with regular activity and subsequent weight reduction may decrease the risk since we know that obese women have a 50%–75% risk of developing type 2 diabetes.

As many as 20% of the women with gestational diabetes tested in the 6–8 week postpartum period will have an abnormal result. The postpartum period is an opportune time to emphasize risk and advise of opportunities to reduce or delay the onset of diabetes and its related complications.

Recommendations and Summary

In conclusion I would like to leave you with the following recommendations for your practice.

Recommendations

- Education from early adolescence
- Maintain healthy lifestyle
- Maintain glycemic control
- Vigilant monitoring and care
- Most effective treatment
- Appropriate postpartum follow-up
- All pregnant women screened for GDM—
use glucose testing if risk \geq average

Respected authorities recommend that education about preconception care for all women of childbearing age who have diabetes will maximize positive outcomes. They recommend the need to stress maintenance of a healthy lifestyle; including normal body weight, healthy diet, and exercise. We have also heard the recommendations and rationale for maintaining tight glycemic control before, during and following pregnancy.

Vigilant monitoring and care of mother and fetus is required by the entire healthcare team.

Appropriate postpartum follow-up is necessary to detect previously undiagnosed type 2 diabetes.

It is important to educate all women about the risk of gestational diabetes (preferably from early adolescence), to screen all pregnant women for gestational diabetes, and to use glucose testing if risk factors are average or above average.

Summary

- ❑ Diabetes increases risk of most common complications of pregnancy and birth defects
- ❑ Advances in screening, diagnosis, and care have lowered infant mortality substantially
- ❑ Vigilant care and glycemic control before, during, and after pregnancy can reduce major complications
- ❑ Most effective therapy for controlling fasting and postprandial blood glucose should be identified and used

To summarize:

- ❑ diabetes increases the risk of most common complications of pregnancy;
- ❑ advances in screening, diagnosis, and care have lowered infant mortality from 25% in the 1960s to 2% in the 1980s;
- ❑ vigilant care before, during, and after pregnancy can reduce major complications of diabetes for both the mother and fetus/neonate; and
- ❑ the most effective therapy for controlling fasting and postprandial blood glucose should be identified and used throughout the continuum of care.

Thank you for participating in this
presentation.

Click the "Post-Test"