Certificate Course in

Gestational Diabetes Mellitus

Cycle I

(AUGUST 2013 – NOVEMBER 2013)

Module I

Introduction to Diabetes in Pregnancy
Disclaimer

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Introduction to Certificate Course in Gestational Diabetes Mellitus

Learning Objectives

Introduction to Diabetes in Pregnancy

Presentations:
- Historical Perspective of GDM
- Pathogenesis of GDM
- Risk Factors of GDM
- Implications of GDM
- Epidemiology of GDM

Primer to Module II

Contents
Introduction to Certificate Course in Gestational Diabetes Mellitus (CCGDM) Cycle I

On behalf of Public Health Foundation of India and Dr. Mohan’s Diabetes Education Academy, we wish you a warm welcome to the Certificate Course in Gestational Diabetes Mellitus (CCGDM)-Cycle I. We congratulate you on having been selected to undergo this course and thank you for agreeing to spare your valuable time to ensure the success of this course.

The CCGDM is designed to equip general practitioners, physicians and obstetricians / gynecologists with the information and tools needed to manage Gestational Diabetes Mellitus (GDM) and pre-existing diabetes in pregnancy in a clinical setting. The Course will be delivered on a Modular basis. There are four Modules, each of which will be delivered on a fixed Sunday every month.

The Modules consist of:

- Pre-test
- Learning objectives
- Teaching slides
- Case studies
- Take home messages
- Post test
- Primer to Next Module

The day’s discussions start with listing of the learning objectives. You can help in making the session more interactive by presenting interesting cases you have seen in your practice.

This is then followed by the pre-test. This consists of ten multiple choice questions (MCQs) based on the topic to be covered during the particular session. This is designed to assess the trainees’ baseline knowledge. The same set of MCQs will be administered as the post-test at the end of the session, following which your facilitator will discuss the answers with you.
The teaching slides have been designed to be as interactive as possible. A number of case studies have also been interspersed among the slides. Please remember that there may not be any “right” or “wrong” answer for many of these; they are only meant to provoke thought and discussion.

In addition to the pre-test and post-test, you are also expected to submit certain Interim Assignments at specified points of time during the course. These are as follows:

- **Assignment 1 (to be submitted during Module III)**
  Compare and contrast the various criteria for the diagnosis of GDM. Which of these do you think is the most ideal one for your practice?

- **Assignment 2 (to be submitted during Module IV)**
  Describe how you would monitor and manage a 24 year old primigravida with GDM, who has failed to reach glycemic goal after two weeks of lifestyle modification.

There will also be an Exit Exam of 50 MCQs at the completion of Module IV, a minimum of 50 % marks is required to pass, which will be one of the criteria for award of the certificate. Further details will be communicated to you closer to the date of the Exam.

The Curriculum for the CCGDM has been designed with inputs from eminent Endocrinologists, Diabetologists and Obstetricians / Gynecologists who have agreed to act as the National Expert Panel for this Course. We are thankful to them for sharing their valuable time and invaluable expertise in designing this course. Even though all efforts have been made to ensure that the information provided is accurate and up to date, you may occasionally come across instances where this is not so. We request you to point these errors and omissions to us so that we can rectify them in time for the Cycle II.

**Further Reading**


*We are sure that you will find this Course Interesting, Enjoyable & Informative!*
Learning Objectives

- Learn about the evolution of the concept of diabetes in pregnancy
- Review the metabolic alterations occurring in pregnancy and how these can lead to diabetes
- Define GDM and discuss its epidemiology
- Learn about the consequences of GDM to the mother and fetus
History of Diabetes in Pregnancy

Until the middle of the 19th century, diabetes was thought to be incompatible with successful pregnancy. Blott, writing in Paris in 1856, concluded that “true diabetes was inconsistent with conception”. This statement was probably linked to the short life expectancy of women with type 1 diabetes in the days before insulin was discovered, meaning that their chances of surviving long enough to reach reproductive age were negligible.

Even in those women who managed to conceive, death from uncontrolled diabetes during or soon after pregnancy was exceedingly common. The dire outlook for women with pre-existing diabetes did not change until a few years after the discovery of insulin, when the subspeciality of diabetes in pregnancy was created following the efforts of Priscilla White and other pioneers.

The concept of “Gestational Diabetes” that is, diabetes occurring on account of the pregnancy itself, dates back to the middle of the 19th century. In 1823 a German physician, Bennewitz, described a single case in whom diabetes developed following conception, only to disappear after delivery (her baby weighed 12 pounds at birth and was said to be “robust and healthy”).

The term “Gestational Diabetes” was first used by O’Sullivan in 1961, following the lead of Hoet from Belgium who used the term “Metagestational Diabetes”.

Definition of Gestational Diabetes Mellitus (GDM)

Gestational diabetes is defined as “glucose intolerance of varying severity with onset or first recognition during pregnancy”. This definition does not discount the possibility that diabetes could have existed prior to the pregnancy. Therefore we can have different categories of women clubbed together under this definition:

- Normal glucose tolerance prior to pregnancy which becomes abnormal with pregnancy and returns to normal following delivery (“True GDM”)
- Mild glucose intolerance (“pre-diabetes”) before pregnancy which worsens during pregnancy
- Previously undiagnosed type 2 diabetes
- Previously undiagnosed type 1 diabetes (rare)

As will be seen from the subsequent discussions, it is important to differentiate gestational diabetes form pre-existing diabetes in pregnancy.
Pathogenesis of Diabetes in Pregnancy

Metabolic Alterations Occurring During Pregnancy

During pregnancy, maternal intermediary metabolism undergoes major changes, most of which are designed to provide a continuous supply of energy and nutrients to the growing fetus while also meeting the nutritional requirements of the mother.

From the metabolic standpoint, pregnancy can be divided into two distinct halves:

- During the first half of pregnancy, there occur changes that promote storage of energy and nutrients. At this point, there is increased appetite combined with normal or increased insulin sensitivity. This promotes storage of energy in the form of fat. These accumulated energy reserves can then be used during the second half of pregnancy to meet the demands of the rapidly growing fetus.

- In the second half of pregnancy, there develops a state of insulin resistance in the mother, facilitating preferential supply of glucose to the growing fetus. Insulin resistance reduces the uptake of glucose by maternal tissues such as white adipose tissue and skeletal muscle, and diverts glucose to the fetus. The mother’s energy requirements are met using alternate fuels such as free fatty acids and ketone bodies. Increased uptake of glucose by the fetus leads to low maternal fasting plasma glucose levels. Human Placental Lactogen (HPL) secreted by the placenta is the main driver of insulin resistance in pregnancy. Other hormones implicated include cortisol, prolactin, and progesterone.

Intermediary metabolism in late pregnancy has been described as an exaggeration of the normal swings between fed-state anabolism and fasting catabolism that occur in nonpregnant individuals. During feeding, glucose and insulin concentrations increase rapidly as a result of the marked insulin resistance and compensatory hyperinsulinemia. Following a period of no calorie intake, blood glucose levels fall much more rapidly than in nonpregnant individuals and insulin release is suppressed. This leads to accelerated lipolysis and ketone body formation (“accelerated starvation”)

**Pathogenesis of GDM**

GDM develops when the maternal pancreatic beta cell is unable to compensate for the insulin resistance of late pregnancy by increasing its output of insulin. While the exact nature of the beta cell defect remains unknown, the following factors may play a role.

- Genetic factors
- Chronic insulin resistance preceding pregnancy (which would have already worn out the beta cell)
- Subclinical inflammation

*Since insulin resistance develops only during the second trimester of pregnancy, GDM is very unlikely to develop before this time. Diabetes diagnosed during the first trimester usually indicates pre-existing type 2 diabetes rather than GDM.*

**Risk Factors for GDM**

The following have conventionally been considered to be risk factors for GDM:

- Obesity
- Metabolic syndrome/diabetes in first degree relative
- Previous macrosomic baby
- Member of high risk ethnic group
- Age > 25 years
- Polycystic ovarian syndrome (PCOS)
- Polyhydramnios in previous pregnancy
- Previous unexplained perinatal loss/birth of malformed baby

From the above list it can be seen that many of the risk factors for GDM are also risk factors for type 2 diabetes. Also, women of Asian Indian origin are at high risk of GDM even if they do not have any of the other risk factors.

**Implications of GDM**

GDM is associated with a host of adverse maternal and fetal implications.

<table>
<thead>
<tr>
<th>Maternal Implications</th>
<th>Fetal Implications</th>
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<td>Pre-eclampsia</td>
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<td>Risk of future diabetes</td>
<td>(Hypoglycemia, hyperbilirubinemia, polycythemia, hypocalcemia)</td>
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<td></td>
<td>Future risk of diabetes and metabolic syndrome</td>
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</table>
Pre-eclampsia

Women with diabetes during pregnancy are at an increased risk of developing pre-eclampsia. This may be due to insulin resistance or may be associated with a combination of genetic factors, advanced age and high BMI. The rate of pre-eclampsia has been shown to be related to the severity of diabetes.

Risk of Future Diabetes in the Mother

GDM can be regarded as an unmasking of future type 2 diabetes. Following delivery, diabetes usually resolves in most women with GDM but it may persist in 5% to 10%. Another 35% to 60% of these women will develop type 2 diabetes within the next decade. Conversion to diabetes occurs more rapidly and more frequently in high risk ethnic groups such as Asian Indians.

Macrosomia

A macrosomic baby (or “large for gestational age”) is defined as one whose weight is above the 90th percentile for the gestational age. While the western guidelines use a cut-off birth weight of 4.5 kg to define macrosomia, 3.5 kg seems reasonable in the Indian setting.

There are two types of macrosomia- symmetrical and asymmetrical. Infants of mothers with GDM have asymmetrical macrosomia with abnormal thoracic and abdominal circumference, which is larger than the head circumference. Organomegaly is also present .

A macrosomic baby has a high risk of sustaining birth injury such as Erb’s palsy, facial palsy, clavicle fracture and humerus fracture. The risk of shoulder dystocia is also high. Women whose babies are large for gestational age are also more likely to go in for cesarean section. In the long run, individuals who were LGA at birth have a high risk of developing type 2 diabetes in later life.

The pathogenesis of macrosomia is best explained by the Pedersen- Freinkel hypothesis. The maternal blood flowing through the placenta is the sole source of glucose and energy for the fetus. Glucose freely passess across the placental barrier down its concentration gradient. This means that higher the maternal blood glucose, more the glucose received by the fetus. The fetal pancreas responds to this excess supply of glucose and other nutrients (“mixed nutrients”) by secreting more insulin. Hyperinsulinemia, in association with plentiful supply of nutrients, leads to excess growth of fetal tissues and consequently, macrosomia.

It therefore follows that maintaining good control of blood glucose in the mother can limit nutrient transfer to the fetus and minimize the risk of macrosomia.

**Figure 1.2**

Fig. 1.2: The Pedersen hypothesis (modified by Freinkel) suggests that macrosomia develops from excess supply of glucose and other nutrients (“mixed nutrients”) to the fetus, and consequent hypersecretion of insulin by the fetal pancreas.
Hypoglycemia

Neonatal hypoglycemia is a major metabolic problem faced by infants of women with poorly controlled diabetes (GDM or pre-existing diabetes). As mentioned above, high levels of maternal blood glucose promote hyperinsulinemia in the fetus, which persist for some time even after the umbilical cord has been clamped and the supply of glucose terminated. This mismatch between glucose supply and insulin levels can lead to hypoglycemia in the neonatal period, which is usually transient.

Other Metabolic Problems in the Neonate

- Polycythemia occurs due to chronic intrauterine hypoxemia and placental insufficiency secondary to poor glycemic control
- As these excess RBCs break down, hyperbilirubinemia occurs days to weeks after birth
- The exact mechanism of hypocalcemia is unknown but may be related to functional hypoparathyroidism

Respiratory Distress Syndrome

Infants of women with poorly controlled diabetes have delayed maturation of their lungs. Pulmonary surfactant production is found to be decreased due to a combination of hyperglycemia and hyperinsulinemia. Management of RDS in these babies is complicated by the fact that use of antepartum steroids for accelerating lung maturity may worsen diabetes control in the mother.

Still Births

The rates of stillbirth are higher in GDM than in the non-diabetic population. The risk of stillbirth depends on the severity of diabetes and adequacy of glycemic control. If the mean blood glucose levels are kept between 105-110 mg/dl, the rate of stillbirth approximates that of the non-diabetic population.

The main causes for stillbirth in GDM are:
- Excess fetal growth secondary to hyperglycemia and hyperinsulinemia
- Fetal growth restriction
- Congenital anomalies are a rare cause of stillbirth in GDM

*Congenital anomalies are rare in GDM, since organogenesis is complete at the time at which GDM usually develops.*

Risk of Future Diabetes in the Offspring

Studies in Pima Indians and other ethnic groups have shown that infants exposed to maternal hyperglycemia during gestation have a high risk of developing type 2 diabetes in later life. Their risk of developing other components of the metabolic syndrome, such as hypertension, central obesity and low high density lipoprotein (HDL) cholesterol were also found to be high.
Epidemiology of GDM

It is difficult to give a single accurate figure for the worldwide prevalence of GDM, since data is lacking from many parts of the world, and different authors have used different tests and varying criteria for the diagnosis of the condition. Nevertheless, it is clear that the prevalence of GDM varies in direct proportion to the prevalence of type 2 diabetes and impaired glucose tolerance (IGT) in a population. From the available literature, the prevalence rates of GDM in different countries vary from <1% to more than 15%.

Data on the prevalence of GDM in India is scanty, but the available literature shows a clear increasing trend in prevalence. The prevalence rates increased from 2% in 1982 to 7.6% in 1991 and 16.5% in 2002. In a multicentric study from India, the highest prevalence of GDM was found in Tamil Nadu and the lowest in Kashmir. With the increasing prevalence of type 2 diabetes and IGT in India, the numbers of women with GDM (and pre-existing diabetes complicating pregnancy) can also be expected to go up further.

Take Home Messages

- Pregnancy is a diabetogenic state
- GDM results when the beta cell is unable to adapt to the diabetogenic milieu of pregnancy
- The prevalence of GDM is high in India
- Diabetes in pregnancy is associated with serious consequences to the baby as well as the mother, if early detection and appropriate treatment are not offered
Module I: Introduction to Diabetes in Pregnancy

LEARNING OBJECTIVES

- Learn about the evolution of the concept of diabetes in pregnancy
- Review the metabolic alterations occurring in pregnancy and how these can lead to diabetes
- Define GDM and discuss its epidemiology
- Learn about the consequences of GDM to the mother and fetus
Notes: 

DIABETES IN PREGNANCY

The Early Days

Pre–insulin era

- Pregnancy in untreated diabetes was almost unknown
- “True diabetes was inconsistent with conception” (Blott, Paris, 1856)- a statement probably prompted by the short lifespan of women with type 1 diabetes (the major cause of pre-gestational diabetes in women of reproductive age in that era)
- Major risk was the death of the mother during, or soon after, pregnancy due to uncontrolled diabetes
- However, overall maternal mortality was also high in that era; it is difficult to tease out the contribution of diabetes to this state of affairs

Module I: Introduction to Diabetes in Pregnancy
Module I: Introduction to Diabetes in Pregnancy

Certificate Course in Gestational Diabetes Mellitus

DIABETES AND PREGNANCY
The Concept of Gestational Diabetes

While the first case of “GDM” was reported by Bennewitz in Germany in 1853 (he considered diabetes a “symptom of pregnancy” and noted that glycosuria resolved after delivery), the concept itself is relatively recent.

Notes: __________________________________________________________________________

Certificate Course in Gestational Diabetes Mellitus

- 1940s - First recognition that maternal hyperglycemia influences pregnancy outcomes
- 1952 - Jorgen Pedersen puts forward the hyperglycemia - hyperinsulinemia hypothesis to explain fetal macrosomia (later termed the Pedersen Hypothesis)
- 1961 - John B. O’Sullivan introduced the term “Gestational Diabetes Mellitus” (GDM)
- 1964 - O’Sullivan and Mahan criteria for diagnosing GDM introduced; these were later modified by Carpenter and Coustan
- Early 1970s - Norbert Freinkel introduces the terms “facilitated anabolism” and “accelerated starvation”

Notes: __________________________________________________________________________
1999 - WHO criteria for diagnosis of GDM introduced
2005 - ACHOIS Study underlined the benefits of treating GDM
2006 - DIPS Guidelines published
2008 - HAPO Study findings published
2010 - IADPSG revises the diagnostic criteria for GDM
2012 - ADA endorses IADPSG Criteria
2013 - NIH states that more evidence is needed before IADPSG criteria are adopted

Gestational Diabetes Mellitus

Definition

“Glucose intolerance of any severity with onset or first recognition during pregnancy”

Metzger BE et al. Diabetes Care, 1998

Contd...
GESTATIONAL DIABETES MELLITUS

**Definition**

- This definition is applicable irrespective of whether insulin is used or not for treatment
- It is also applicable irrespective of whether the condition resolves after delivery
- It does not exclude the possibility that diabetes could have antedated the pregnancy

**Contd...**

Women diagnosed with GDM might have:

- Normal glucose tolerance prior to pregnancy which becomes abnormal with pregnancy and returns to normal following delivery
- Mild glucose intolerance (“pre-diabetes”) before pregnancy which worsens during pregnancy
- Previously undiagnosed type 2 diabetes
- Previously undiagnosed type 1 diabetes (rare)
EFFECT OF PREGNANCY ON BLOOD GLUCOSE

- Pregnancy is characterised by profound metabolic alterations in the mother
- The main purpose of these changes is to ensure adequate nutrition (in the form of glucose) to the growing fetus during times of plenty as well as times of scarcity
- At the same time, the metabolic demands of the mother also need to be met
MATERNO - FETAL NUTRIENT TRANSFER

- The fetus is dependent on the maternal supply of nutrients for all its requirements.
- Nutrients from the maternal circulation cross the placental barrier and reach the fetus.
- This process is primarily dependent on the materno-fetal concentration gradient of the nutrient in question.

Glucose and amino acids traverse the placenta while insulin does not.

(Freinkel N. Diabetes, 1980)
Metabolism during pregnancy is best described as a combination of “facilitated anabolism” and “accelerated starvation (catabolism)”

**EARLY PREGNANCY**

**Facilitated Anabolism**

- Main hormones involved are estrogen and progesterone
- These hormones cause hyperinsulinemia by promoting beta cell hyperplasia and increased insulin release
- During early pregnancy, the first phase insulin secretion is found to be augmented when compared to pre-gravid state; however, second phase secretion remains unchanged

Note: The figure schematically represents maternal metabolic changes during gestation. Anabolism during feeding and catabolism during fasting are exaggerated in a progressive fashion, reflecting the combined effects of placental hormones and nutrient use by the fetus.
**EARLY PREGNANCY**

**Facilitated Anabolism**

- Hyperinsulinism
- Increased insulin sensitivity
- Increased glycogenesis
- Reduced hepatic glucose output
- Increased peripheral glucose uptake
- Increased lipid synthesis

This leads to a reduction in fasting plasma glucose levels in early pregnancy.

**Contd…**

**Notes:** During early pregnancy, insulin resistance is low while beta cell function is normal or increased. This leads to low plasma glucose levels as well as HbA1c till around the 20th week of pregnancy. The placental transfer of glucose to the growing fetus is another important reason for lowering of maternal glucose levels.
EARLY PREGNANCY

Since insulin sensitivity is normal or raised during early pregnancy and insulin secretion is increased, GDM is rare during this period

Women diagnosed to have “GDM” during early pregnancy may have had hitherto undiagnosed type 2 diabetes

LATER PREGNANCY

Stage of Insulin Resistance

- After 20 weeks of gestation, the placental hormones start playing an increasingly important role
- The main placental hormone contributing to insulin resistance is human placental lactogen (HPL)
- Other hormones involved are prolactin, cortisol, progesterone and growth hormone
- All of these hormones antagonise the effect of insulin and bring about a state of physiological insulin resistance
**Module I: Introduction to Diabetes in Pregnancy**

**Certificate Course in Gestational Diabetes Mellitus**

**LATER PREGNANCY**

**Stage of Insulin Resistance**

- Increased levels of placental hormones
- Insulin resistance

- Facilitated diffusion following a meal
  - Higher blood glucose levels enable free diffusion to fetus to meet its increased demands

- Accelerated starvation in the fasting state
  - High levels of free fatty acids and ketone bodies to provide fuel for the mother, so that glucose is spared for the fetus

**Slide 21**

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**Notes:**

- Buchanan TA et al, Diabetes Rev, 1995

First-phase insulin response (minutes 1–10 of intravenous glucose tolerance test) in normal women and women who developed GDM

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**Slide 22**

**Note:** Buchanan and Catalano used euglycemic, hyperinsulinemic clamps and intravenous glucose tolerance tests to measure insulin sensitivity and secretion in normal women and in those with GDM before and during early and late pregnancy. Their results demonstrate increasing insulin secretion in both groups, but a much flatter slope in the women with GDM [despite the fact that insulin resistance was somewhat greater in the women with GDM]
Insulin sensitivity during different stages of pregnancy in women with and without GDM

PATHOGENESIS OF GDM

- In most women, the beta cell can compensate for the increased insulin resistance of pregnancy by hyperplasia and hypertrophy (Van Assche et al, 1978)
- Third trimester fasting insulin levels are 2 fold higher than pre-pregnant levels in normal pregnant women
- This results in fasting blood glucose levels that are 10 to 20 mg/dl lower than in the nonpregnant state, even in the last trimester (Kalhan SC, 1979; Metzger BE, 1982; Buchanan TA, 1990; Catalano PM, 1992)

GDM develops when the beta cell is unable to compensate for the increased insulin resistance

Note: Although insulin secretory defect (failure of compensation) underlies most cases of GDM, it is also noteworthy that women with GDM tend to have lower insulin sensitivity during all stages of pregnancy as well as in the pre-gravid state.
WHY DOES THE BETA CELL FAIL TO ADAPT?

- Genetic factors
- Chronic insulin resistance antedating pregnancy (especially in obese women)
- Subclinical inflammation

RISK FACTORS OF GDM
GDM
Risk Factors

- Obesity (BMI >25) and Metabolic syndrome
- Diabetes in first degree relative
- Previous GDM or glucose intolerance
- Previous macrosomic baby
- Member of high risk ethnic group (all Indians fall in this category)
- Age >25
- Polycystic Ovarian Syndrome (PCOS)
- Previous polyhydramnios
- Previous unexplained perinatal loss or birth of a malformed infant

Note: The risk factors for GDM are listed above. It can be easily appreciated that most pregnant women will have one or more of these risk factors.

IMPLICATIONS OF GDM

Notes: ________________________________
IMPLICATIONS OF GDM

Maternal implications

- Pre-eclampsia
- Polyhydramnios
- Operative delivery
- Perineal trauma
- Risk of future diabetes

Fetal and Neonatal implications

- Fetal macrosomia
- Birth trauma
- Prematurity
- Neonatal metabolic complications (hypoglycemia, hyperbilirubinemia, hypocalcemia, polycythemia)
- Obesity and diabetes in later life

Congenital malformations are extremely uncommon in GDM, since it usually develops in late pregnancy, long after organogenesis is complete.

Risk of malformation is similar to that in women with pre-existing diabetes if GDM is diagnosed in the first trimester.
MACROSOMIA

- A macrosomic baby is one whose weight is above the 90th percentile for the gestational age
- Also termed “large for gestational age (LGA)”
- The American College of Obstetricians and Gynecologists prefers a cut off of 4.5 kg to define a macrosomic baby
- No validated cut offs for India - 3.5 kg seems reasonable (3.45 kg corresponds to the 90th percentile of birth weight for Indians)

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MACROSOMIA

- There are two types of macrosomia - symmetrical and asymmetrical
- Infants of mothers with GDM have asymmetrical macrosomia with abnormal thoracic and abdominal circumference which is larger than head circumference
- Organomegaly is also present
- In untreated GDM, the risk of macrosomia is as high as 40% (Persson and Hanson, Diabetes Care, 1998)

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Notes: 
MACROSOMIA

- High risk of birth trauma (shoulder dystocia, clavicle fracture, humerus fracture, brachial palsy, facial palsy)
- Increased risk of C-section
- Increased risk of diabetes in later life

PATHOGENESIS OF MACROSOMIA

The Pedersen Hypothesis

Maternal hyperglycemia leads to excess exposure of the fetus to maternal glucose, fetal hyperinsulinemia, and excess growth

This concept was further refined by Freinkel, who added a potential role of other nutrients (“mixed nutrients”) in fetal overgrowth
PATHOGENESIS OF MACROSOMIA
The Pedersen - Freinkel Hypothesis

Note: The Pedersen hypothesis, later modified by Freinkel, suggests that macrosomia results from excess supply of glucose and other nutrients (“mixed nutrients”) to the fetus, and consequent hypersecretion of insulin by the fetal pancreas. (Freinkel N, Diabetes, 1980)

OTHER METABOLIC PROBLEMS IN THE NEONATE

Hypoglycemia
This occurs due to abrupt cessation of delivery of maternal glucose to a neonate whose insulin levels are high following exposure to chronic maternal hyperglycemia during pregnancy.
NEONATAL HYPOGLYCEMIA IS INVERSELY RELATED TO MATERNAL HYPERGLYCEMIA AT DELIVERY

Therefore good control of maternal diabetes can prevent neonatal hypoglycemia

**Note:** In any form of diabetes in pregnancy, the higher the maternal plasma glucose levels at delivery, the greater the risk of hypoglycemia in the neonate. (Jovanovic L, Peterson CM. Am J Med, 1983)

OTHER METABOLIC PROBLEMS IN THE NEONATE

- **Polycythemia** occurs due chronic intrauterine hypoxemia and placental insufficiency secondary to poor glycemic control
- As these excess RBCs break down, **hyperbilirubinemia** occurs days to weeks after birth
- The exact mechanism of **hypocalcemia** is unknown but may be related to functional hypoparathyroidism (Tsang J et al, J Pediatr, 1975)
IMPAIRED FETAL LUNG MATURATION
Respiratory Distress Syndrome

- In a diabetic pregnancy, lung maturation is delayed due to reduced surfactant production secondary to hyperglycemia and hyperinsulinemia
- Poorly controlled diabetes in pregnancy is an important risk factor for RDS

STILLBIRTHS

- Stillbirth rate in GDM is greater than that of the general population
- Majority occur even in the absence of congenital malformations
- Depends on the severity of diabetes and adequacy of metabolic control
- Rate of stillbirth is equal to that in the general population if mean blood glucose levels can be kept below 105-110 mg/dl
- Mainly related to excess fetal growth, consequent to hyperglycemia and hyperinsulinemia (Pettitt et al, Diabetes Care, 1980)
- However, fetal growth restriction can also contribute to stillbirths
Good control of glucose levels in the mother can reduce all adverse pregnancy outcomes in GDM.

This is one of the cornerstones of modern GDM management.

GDM AND RISK OF FUTURE DIABETES IN THE OFFSPRING

Infants of mothers who had diabetes during pregnancy have a higher risk of developing obesity, metabolic syndrome and IGT/ type 2 diabetes in the future.

*Dabelea D, Diabetes Care, 2007*

Offspring of women with GDM are at 4 to 8 times higher risk of developing type 2 diabetes.

*Clausen TD, Diabetes Care, 2008*

Contd...
GDM AND RISK OF FUTURE DIABETES IN THE OFFSPRING

![Graph showing prevalence of type 2 diabetes by age-group in offspring of diabetic, pre-diabetic, and nondiabetic mothers.](image)

Note: The Figure shows the prevalence of type 2 diabetes by age-group in offspring of diabetic (women who had diabetes before or during pregnancy), pre-diabetic (those who developed diabetes after pregnancy), and nondiabetic mothers. By age 5–9 and 10–14 years, diabetes was present almost exclusively among the offspring of diabetic women. In all age-groups, there was significantly more diabetes in the offspring of diabetic women than in those of pre-diabetic and nondiabetic women. There were much smaller differences in diabetes prevalence between offspring of pre-diabetic and nondiabetic women. (Dabelea D, Pettitt DJ. Pediatr Endocrinol Metab, 2001)

GDM AND RISK OF METABOLIC SYNDROME IN THE OFFSPRING

![Graph showing risk of metabolic syndrome components in offspring of diabetic and non-diabetic mothers.](image)

Note: Adult health outcomes and exposure to maternal diabetes. The risk of developing one or other of the components of metabolic syndrome in adulthood is higher in infants exposed to maternal diabetes in utero. Even the presence of risk factor for GDM (without overt hyperglycemia) confers excess risk. (Moore TR. Am J Obstet Gynecol, 2010)
IMPLICATIONS TO THE MOTHER
Pre-eclampsia

- Diabetic pregnancy is associated with a higher rate of hypertensive complications than normal pregnancy
- Risk of pre-eclampsia is increased in GDM (15%-20% vs. 5%-7% in non-GDM)
- This is due to a combination of insulin resistance, genetic factors, age and BMI


The rate of pre-eclampsia depends on the severity of GDM

*Yoge Y, Am J Obstetr Gynecol, 2004*

**Note:** The figure shows the rate of pre-eclampsia in relation to the severity of GDM, as assessed by fasting plasma glucose. Higher the FPG, more the prevalence of PET. (Yoge Y. Am J Obstet Gynecol, 2004)
IMPLICATIONS TO THE MOTHER
Risk of Future Diabetes

- Following delivery, diabetes persists in 5% to 10% of women diagnosed to have GDM
- 35% to 60% of women with GDM will develop type 2 diabetes within 10 years
- Conversion to diabetes occurs more frequently, and faster, in high risk ethnic groups (such as Asian Indians)

Tovar A et al. Prev Chronic Dis, 2011

EPIDEMOIOLOGY OF GDM

Supported by an educational grant from Johnson & Johnson MEDICAL COMPANIES
EPIDEMIOLOGY OF GDM

Global Scenario

- Prevalence of GDM varies according to the population studied, test used, timing of testing and criteria used
- Global prevalence rates vary from 1% to >15%
- The prevalence rate of GDM in a population is proportional to that of diabetes and IGT in that population (King, Diabetes Care, 1998)

EPIDEMIOLOGY OF GDM

Indian Scenario

- Prevalence of GDM is steadily rising in India
- The rates increased from 2% in 1982 (Agarwal and Gupta) to 7.6% in 1991 (Narendra) and 16.55% in 2002 (Seshiah)
- In a multicentric study in India, the highest prevalence of GDM was found in Tamil Nadu and the lowest in Kashmir (Seshiah et al, 2004)
GDM is more prevalent in the urban areas and among older and more obese women

**Note:** A study conducted in 11,256 pregnant women in Tamil Nadu showed that the urban areas had the highest prevalence rates of GDM compared to semi-urban and rural areas. The prevalence of GDM increased with increasing age and BMI of the mother. (Seshiah et al, J Assoc Physicians India, 2008)

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**TAKE- HOME MESSAGES**

- Pregnancy is a diabetogenic state
- GDM results when the beta cell is unable to adapt to the diabetogenic milieu of pregnancy
- The prevalence of GDM is high in India
- Diabetes in pregnancy is associated with serious consequences to the baby as well as the mother, if early detection and appropriate treatment are not offered

**Notes:**
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**MODULE II**

*Screening and Diagnosis of GDM*

- Screening for GDM
- Diagnosis of GDM
- Pre-existing diabetes and pregnancy
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Notes: