

Gestational Diabetes Mellitus

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Diabetes in Pregnancy

Pre-gestational and Gestational

The Importance of GDM

2 Generations at Risk

- ❖ Women with h/o GDM of developing T2 DM in the future
- ❖ Offspring: Fetal / neonatal morbidity
increased future risk of diabetes and obesity

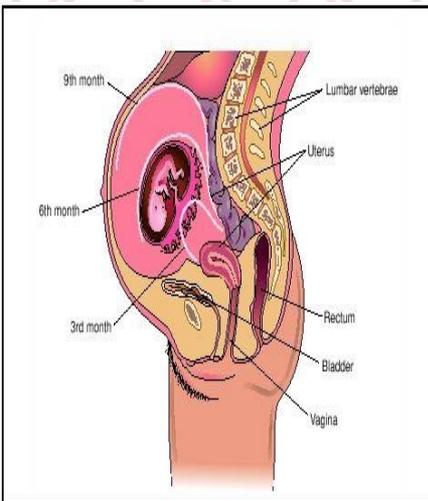
Pregnancy is a period in which short term intensive care gives a long term pay off in the primary prevention of obesity, IGT and diabetes in the offspring.....

preventive medicine starts before birth

Normal Pregnancy- A Great Metabolic Stress Test

Metabolic goals of pregnancy

- 1) Early pregnancy -develop anabolic stores (anti-insulin hormones)
- 2) Late pregnancy -provide fuels for fetal growth (maternal hepatic glucose output)



↓

Physiological Insulin Resistance

↓

Compensatory Hyperinsulinemia

Normal maternal metabolic adaptation

mean FPG: **74.5 ± 11 mg/dl**

PP peak: **108.7 ± 16.9mg/dl**

When Does GDM Develop?

A pregnant woman who is not able to increase her insulin secretion to overcome the insulin resistance that occurs even during normal pregnancy

Maternal hyperglycemia



Fetal hyperglycemia



Fetal hyperinsulinemia



Case

Sita, 22 yo

1st antenatal visit

Primi

16 weeks gestation

No significant past medical history/ family history

Pre-pregnancy BMI : 21 kg/sq mt

Q. Would you screen for GDM now?

1. Yes

2. No

Case

Sita, 22 yo

1st antenatal visit

Primi

16 weeks gestation

No significant past medical history/ family history

Pre-pregnancy BMI : 21 kg/sq mt

Q. Would you screen for GDM now?

1. Yes

2. No

Universal GDM Screening

- Indian women have 11 fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women

- **Prevalence of GDM in India : 13.9% (WHO criteria)**

As routine screening for GDM is not done, probably the undiagnosed glucose intolerance that has been occurring in the past has resulted in the increased prevalence of diabetes in India.

Gestational Weeks at Which Screening is Recommended

- **first trimester**

(fetal beta cell recognizes and responds to maternal glycemic level as early as 16th week of gestation)

If found negative at this time -

- **around 24th – 28th week**

- **finally around 32nd – 34th week**

Case

Sita

1st ANC visit

16 weeks gestation

Q. Screening method

- 1. F/PP glucose**
- 2. HbA1c**
- 3. 50 g 1 hour glucose**
- 4. 75 g 2 hour OGTT**
- 5. 100 g 3 hour OGTT**

Case

Sita

1st ANC visit

16 weeks gestation

Q. Screening method

- 1. F/PP glucose**
- 2. HbA1c**
- 3. 50 g 1 hour glucose**
- 4. 75 g 2 hour OGTT**
- 5. 100 g 3 hour OGTT**

Case

Sita

75 g OGTT

2hr glucose- 140 mg/dl

Q. What is your diagnosis?

1. Normal

2. IGT

3. GDM

Case

Sita

75 g OGTT

2hr glucose- 140 mg/dl

Q. What is your diagnosis?

1. Normal

2. IGT

3. GDM

GDM Criteria- ADA

	National Diabetes Data Group*	American Diabetes Association* IADPSG (75 g 2 hr OGTT)	World health Organization †	Carpenter and Coustan* (100 gm 3 hr OGT) 2 or more criteria met
Fasting	105	92 OR	≥ 126	95
1 hour	190	180 OR	-	180
2 hours	165	153	≥ 140	155
3 hours	145	-	-	140

(Based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study)

Indian GDM Screening Criteria - DIPSI (WHO)

One abnormal Value is enough

	International Diabetes Data Group*	American Diabetes Association* IADPSG	World health Organization † (75 g 2 hr)	Carpenter and Coustan*
Fasting	105	92	≥ 126	95
1 hour	190	180	-	180
2 hours	165	153	≥ 140	155
3 hours	145	-	-	140

2 hour 75 gm glucose challenge

- ❖ one step procedure
- ❖ equivalent diagnostic capability
- ❖ simple, economical and feasible

75 gm OGTT (WHO criteria)

In Pregnancy

Outside Pregnancy

2 hr \geq 200 mg/dl

Diabetes

Diabetes

2 hr \geq 140 mg/dl

GDM

IGT

2 hr \geq 120 mg/dl

DGGT

--

‘Decreased Gestational
glucose tolerance’

JAPI - Diabetes in Pregnancy Study Group India (DIPSI) DIPSI Guidelines

DIPSI

DIPSI Guidelines - Kolkata Declaration



Fifth National Conference of Diabetes in Pregnancy Study Group, India

V Seshiah

5th – 7th Feb 2010, Kolkata

“Diabetes Free Generation - Focus on the Fetus for the Future”

“A single step procedure with a single glucose value” to diagnose abnormal glucose tolerance during pregnancy in the community - Indian Guidelines*

Representation from the National Bodies

Diabetes In Pregnancy Study Group India (DIPSI) - Dr V Seshiah, Dr A K Das, Dr V Balaji, Dr Sunil Gupta
Association of Physicians of India (API) - Dr B K Sahay, Dr Siddharth N Shah, Dr Debasis Maji, Dr Shashank R Joshi, Dr A Parneerselvam, Dr N Rajendran
Indian Medical Association (IMA) - Dr S Daga, Dr Samar Banerjee, Dr A Bhavatharani, Dr Madhuri S Balaji
Research Society for the Study of Diabetes In India (RSSDI) - Dr P V Rao, Dr HB Chandalia
Endocrinology Society of India - Dr A Ammini, Dr S K Sharma, Dr A H Zargar
Federation of Obstetrics and Gynecological Societies of India (FOGSI) - Dr H Konnar, Dr Sanjay Gupte, Dr Hema Divakar, Dr Sujata Misra, Dr Uday Thanawala, Dr Cynthia Alexander, Dr Ambarish Bhandiwad, Dr Anjalakshi C

1. Gestational Diabetes Mellitus (GDM)

1.1 Defining the condition and the aim of the declaration:

GDM is a clinical entity associated with a significant incidence of diabetes, in the later life of the mother and an increase in the fetal, neonatal morbidity and future development of obesity and diabetes in the offspring.^{1,2}

Pregnant women belonging to a high risk ethnic population (e.g. Indians) require *Universal Screening*. This observation emphasizes the need for an appropriate diagnostic tool to diagnose and method to treat GDM

criteria. Among them, the overall prevalence of GDM was 13.9%.⁵ Further, to ascertain the consistency of WHO criteria in diagnosing GDM, after determining the desired sample size with the required statistical power, a total of 1246 pregnant women underwent 75g OGTT. Among them 13.2% were detected to have GDM with a 2hr PG \geq 140 mg/dl. This finding substantiates and validates the previous prevalence data as well as the WHO criteria. Thus 2 hour plasma glucose \geq 140 mg with 75 gm oral glucose load has been accepted by the Diabetes in pregnancy Study group India (DIPSI) for diagnosing GDM (our population do not accept diagnosis based on FPG).

1.3 Short Term and Long Term Implications for the Progeny of GDM:

1.3.1 Increased birth weight of neonates was observed even when the mother's glucose tolerance was less than the glycemic criteria recommended by WHO for diagnosing GDM.⁶ The occurrence of macrosomia was continuum as the 2 hour plasma glucose with 75 gm OGTT, increased from 120 mg/ dl.^{7,8}

1.3.2 In children born to mothers who had third trimester plasma glucose 120 - 139 mg/ dl, the cumulative risk of developing type 2 diabetes was 19 % at age 24 years and this risk almost doubled to 30% with respect to those women who had 2 hour plasma glucose 140- 199 mg/ dl.⁹

Case: Congratulations!!

- Sita delivered a 3kg female child
- Mother and baby are both doing well
- She asks you,
 - **“Will I have to continue to take diabetes meds life-long?”**

1. Yes
2. No
3. Maybe

Risk of future T2DM

- **5%-10% of women with GDM develop T2DM immediately postpartum**
- **50% chance of T2DM over next 10-20 years**

Towards a better future ...

- **Counseled for breastfeeding/ self-care/ healthy life style/ Metformin/**
- **Re-evaluate with 75 g OGTT after 6 wk, 6 months and tri-annually; annual FPG**
- **Frequency of screening depends on risk factors including family history, prepregnancy BMI, and need for insulin/OHA during pregnancy.**
- **Contraception**

Thank you



‘No single period in human development provides a greater potential than pregnancy for long range pay off via relatively short range period of enlightened metabolic manipulation’

Norbert Fienkel

Pathophysiology

Pregnancy is Diabetogenic condition
A Wonderful Metabolic Stress Test

Insulin resistance due to placental secretion of anti-insulin hormones

Progesterone, Cortisol, GH

Human Placental Lactogen (HPL), Prolactin

Late pregnancy:

- Maternal hepatic glucose production increases by 15%-30% to meet fetal demand¹

- Beta-cell dysfunction

Gestational diabetes mellitus (GDM)

Pancreatic beta-cell dysfunction caused by:

- Genetics
- Autoimmune disorders

GDM: Etiology and Risk Factors

Etiology

- Hormonally induced insulin resistance
- Resulting in hyperglycemia
- Eventually progresses into diabetes

Gestational diabetes mellitus (GDM) risk factors^{1,2}

- Obesity
- Previous history of GDM
- Prior delivery of a large baby (>9 lbs)
- Glycosuria
- Family history of diabetes in a first-degree relative

Risk of future T2DM

- 5%-10% of women with GDM develop T2DM immediately postpartum⁶
- 35%-60% chance of T2DM over next 10-20 years⁶
- Risk increased with uncontrolled blood sugar in pregnancy⁵

Problems with GDM: Maternal

- **pre-eclampsia**
- **hyperglycemic crisis,**
- **urinary tract infections that may result in pyelonephritis,**
- **need for cesarean sections,**
- **morbidity from operative delivery,**
- **increased risk of developing overt diabetes,**
- **cardiovascular complications later in life, including hyperlipidemia and hypertension.**

Problems with GDM

- **Mothers with GDM have a 50% chance of developing type 2 diabetes mellitus (T2DM) for the 20 years following their diagnosis of GDM.**
- **Maternal hyperglycemia causes increased glucose delivery to the fetus, resulting in fetal hyperinsulinemia and increased fetal growth.**
- **Complications of excessive fetal growth include birth trauma, increased cesarean deliveries, and the long-term risk of glucose intolerance and obesity.**
- **Other immediate fetal complications include hypoglycemia, hyperbilirubinemia, respiratory distress syndrome, cardiomyopathy, and hypocalcemia**

GDM and Co-morbidities

- **Fourfold increased risk of hypertension during pregnancy.**
- **GDM with underlying preexisting moderate-to-severe nephropathy (urine albumin:creatinine ratio ≥ 300) or renal impairment (serum creatinine > 1.4 mg/dL) are at the greatest risk for deterioration**

GDM and Co-morbidities

- **High risk for PDR (retinopathy) at baseline—namely women with diabetes for greater than 10 years, pre-existing moderate-to-severe retinopathy, and poor glycemic control.**
- **Laser coagulation has been shown to be safe and efficacious in pregnancy for the treatment of the pre-proliferative stages of retinopathy.**
- **Prior retinopathy screening is a must**
- **Refractory to laser coagulation, termination of pregnancy can be considered given the high risk of permanent blindness**

GDM and Co-morbidities

- **Pre existing-Gastroparesis is considered a relative contraindication to pregnancy given the significant maternal morbidity and poor reported perinatal outcomes.**
- **Very difficult to manage as pregnancy itself causes the same**
- **Hydration, electrolyte imbalance and prokinetic agents may help**

GDM predisposes to CVD

CIRCULATION AHA.111.044784 Published online before print February 17, 2012, doi: 10.1161/

- **Women who experience pregnancy-related complications, particularly gestational diabetes and preeclampsia, are more likely to develop cardiovascular disease later in life.**
- **In the prospective Avon Longitudinal Study of Parents and Children (ALSPAC), researchers studied the associations of gestational diabetes, preeclampsia, preterm delivery and size for gestational age with calculated 10-year CVD risk and CV risk factors.**

According to study data, gestational diabetes and preeclampsia raised risk for CVD by 26% and 31%, respectively.

Researchers found gestational diabetes had a positive association with fasting glucose and insulin, whereas preeclampsia was associated with higher BMI, waist circumference, blood pressure, lipids and insulin.

The ORs for the calculated 10-year CVD risk based on the Framingham prediction score was 1.31 (95%

**ADA/EASD RECOMMENDATION
STANDARDS OF MEDICAL CARE
IN DIABETES—2013**

Recommendations: Detection & Diagnosis of GDM (1)

- **Screen for undiagnosed T2D at the first prenatal visit in those *with risk* factors, using standard diagnostic criteria.**
- **In pregnant women not previously known to have diabetes, screen for GDM at 24–28 wks' gestation, using a 75-g OGTT & specific diagnostic cut points.**
- **Screen women with GDM for persistent diabetes at 6–12 wks' postpartum, using the OGTT & non-pregnancy diagnostic criteria.**

Criteria for diagnosis of Overt DM

A1C \geq 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

FPG \geq 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h plasma glucose \geq 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

Detection and Diagnosis of GDM (2)

- **Women with a history of GDM:**
 - **Should have lifelong screening for the development of diabetes or prediabetes at least every 3 years.**
 - **Found to have prediabetes should receive lifestyle interventions or metformin to prevent diabetes.**

Diagnosis of Gestational Diabetes

- **GDM carries risks for the mother & neonate.**
- **The HAPO study, demonstrated that risk of adverse maternal, fetal, & neonatal outcomes continuously increased as a function of maternal glycemia at 24-28 wks, even within ranges previously considered normal for pregnancy.**
- **IADPSG, recommended that all women not known to have prior diabetes undergo a 75-g OGTT at 24–28 wks of gestation.**

HAPO: Hyperglycemia & Adverse Pregnancy Outcomes

IADPSG: International Association of Diabetes & Pregnancy Study Groups

Screening for & Diagnosis of GDM

- Perform a 75-g OGTT, with BG measurement fasting & at 1 and 2 h, at 24–28 weeks' gestation in women not previously diagnosed with overt diabetes.
- Perform OGTT in the morning after an overnight fast of at least 8 h.
- GDM diagnosis: when any of the following plasma glucose values are exceeded
 - Fasting ≥ 92 mg/dL (5.1 mmol/L)
 - 1 h ≥ 180 mg/dL (10.0 mmol/L)
 - 2 h ≥ 153 mg/dL (8.5 mmol/L)

These new criteria will significantly increase the prevalence of GDM, primarily because only 1 abnormal value, not 2, is sufficient to make the diagnosis.

Diagnosing GDM

- **A definitive diagnosis of GDM is currently made on the result of an OGTT.**
- **Currently, a two-stage diagnostic procedure is conducted in some parts of the world.**
- **A two-stage procedure involves a non-fasting glucose challenge test (GCT) followed by a formal OGTT for women who have a positive result.**

Risk factors for GDM

- **Severe obesity**
- **Prior history of GDM or delivery of large-for-gestational-age infant**
- **Presence of glycosuria**
- **Diagnosis of PCOS**
- **Strong family history of type 2 diabetes**

Risk for GDM

Very High Risk

- Severe obesity
- Prior history of GDM or delivery of a large-for-gestation-age infant (>4,000 g/4,250 g/4,500 g)
- Presence of glycosuria
- Diagnosis of PCOS
- Strong family history of type 2 diabetes

Low Risk—Must Meet ALL of the Following Criteria:

- Age under 25
- Normal weight prior to pregnancy
- Member of an ethnic group with low prevalence of diabetes
- No known diabetes in first-degree relative
- No history of abnormal glucose tolerance
- No history of poor obstetrical outcomes

Average Risk—Criteria Not Met for High or Low Risk

Source: ADA 2009

Risk and Testing

- **Patients at very high risk for developing GDM should be screened as soon as pregnancy is confirmed using standard diagnostic testing.**
- **If this initial screening is negative, they are considered average risk and should be retested at 24 to 28 weeks of gestation using the one- or two-step approach.**
- **Women with average risk should be tested at 24 to 28 weeks of gestation.**
- **Those who meet all the criteria for low risk do not require testing**

Potential Risks

- **Macrosomia**
- **Brachial plexus injury**
- **Fracture with delivery**
- **Fetal hypoglycemia**
- **Fetal hyperbilirubinemia**
- **Fetal hypocalcemia**
- **Childhood obesity**
- **Neuropsychological outcomes**
- **Development of diabetes**
- **Perinatal mortality**
- **3rd/4th degree lacerations**
- **Instrument deliveries**
- **Cesarean delivery**
- **Preeclampsia**
- **Future diabetes mellitus**



Treatment Approach

- Risk assessment at first PN visit
- Screen those at very high risk immediately
- Otherwise check at 24-28 weeks
- Initial check after 50g oral glucose load-
threshold of 130 or 140 THEN 100gm OGTT
on separate day in those who fail

2011 UPDATE

- The IADPSG were created in 1998 to formulate recommendations for glucose tolerance testing in pregnancy.
- The IADPSG is made up of individuals from a variety of affiliated organizations with a focus on diabetes and pregnancy.
- The panel recommended the 2-h, 75-g OGTT for the diagnosis of GDM with the following thresholds

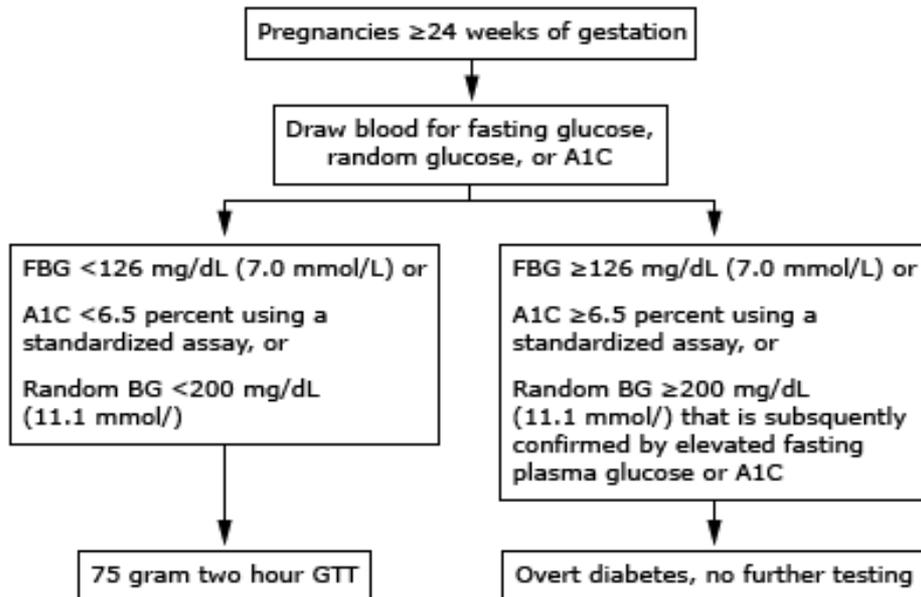
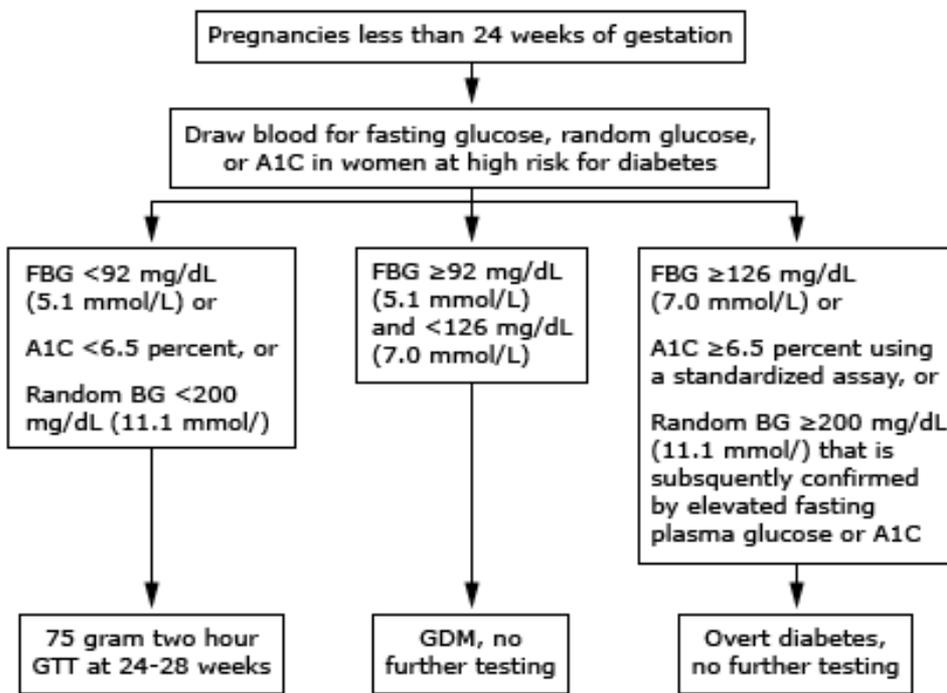
Time	Value + for GDM
<i>Fasting</i>	$\geq 92 \text{ mg}\%$ *
<i>1 hr</i>	$\geq 180 \text{ mg}\%$
<i>2 hr</i>	$\geq 153 \text{ mg}\%$

* After an 8 hour overnight fast

IADPSG

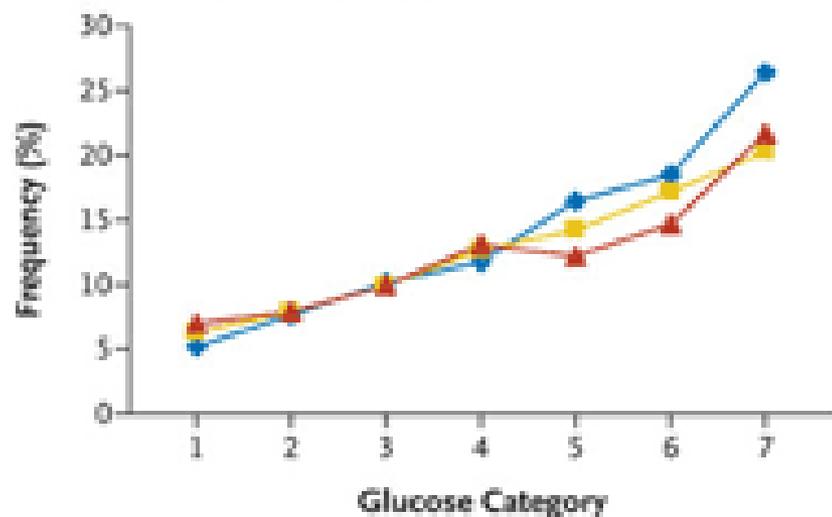
■ International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy.

■ Diabetes Care 2010; 33:676.

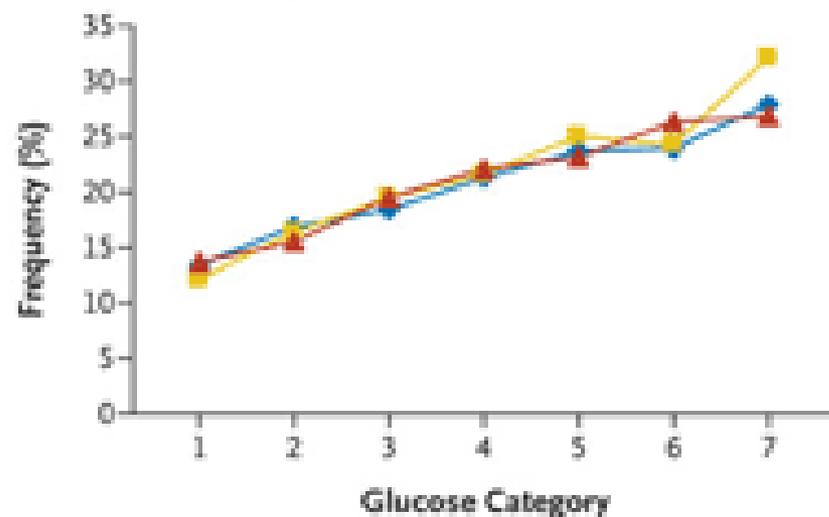


◆ Fasting glucose
 ■ 1-Hr glucose
 ▲ 2-Hr glucose

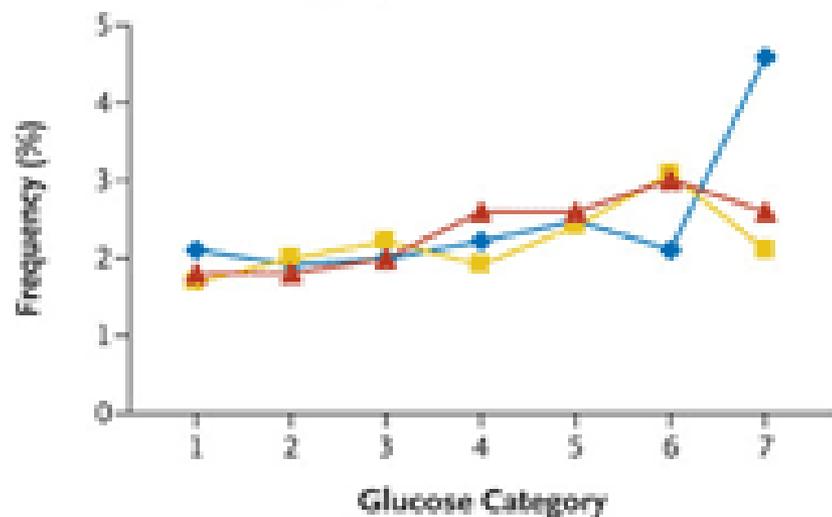
A Birth Weight >90th Percentile



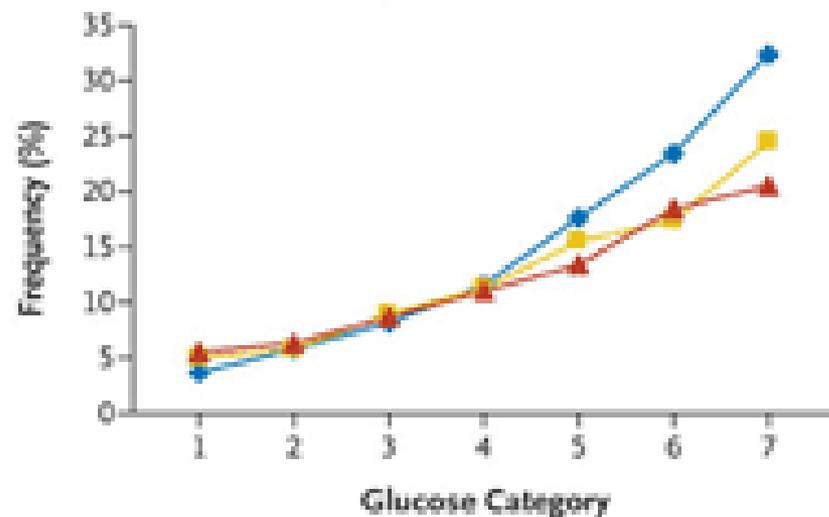
B Primary Cesarean Section



C Clinical Neonatal Hypoglycemia



D Cord-Blood Serum C Peptide >90th Percentile



Overt DM in pregnancy

- In addition, the IADPSG also made recommendations regarding the diagnosis of overt diabetes during pregnancy.
- They recommended that
 - fasting plasma glucose (FPG) ≥ 126 mg/dL ,
 - a hemoglobin A1c (HbA1c; using a DCCT/ UKPDS standardized assay) $\geq 6.5\%$
 - random plasma glucose level ≥ 200 mg/dL (which requires confirmation by FPG or HbA1c) during the first trimester of pregnancy be diagnostic of overt diabetes.

Recommendations

Before pregnancy

- **Particularly important for women who currently have diabetes or intermediate degrees of hyperglycaemia (impaired glucose tolerance – IGT, or impaired fasting glucose – IFG), or have experienced GDM in a previous pregnancy.**
- **The probability of developing GDM in a subsequent pregnancy is of the order of 30% to 50%. If more than a year has passed since the postpartum assessment, then these women should have an oral glucose tolerance test (OGTT) prior to conception or at least in the first trimester.** [Diabetes Care 2007; 30: 1314-9]
- **If the glycaemic status is then normal, the OGTT should be repeated at around 26 to 28 weeks, or at an earlier time if clinically indicated.**

Diabetic control before conception

- **Spontaneous miscarriages appears to be low when the HbA1c is modestly raised, and higher with increasingly poor glycaemic control** [Am J Obstet Gynecol 1987; 156: 1096-100]
- **The same pattern is also found with respect to the rate of fetal malformations.** [Teratology 1989; 39: 225-31]
- **Women with diabetes should be encouraged to obtain the best possible glycaemic control before conception, an HbA1c <6.5% (or <7.0% if on insulin).**
- **Some consensus opinions advocate a lower value and this is reasonable if it can be safely achieved and maintained.**

Managing DM in a pregnancy

- **Whenever it is possible, pregnant women with diabetes should be encouraged to self-monitor blood glucose levels both fasting and postprandial, preferably 1 h after a meal.**
- **The target glucose levels should be as low as possible compatible with patient comfort and safety.**
- **The conclusions of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus, in the absence of specific evidence, referred to ‘upper boundary’ treatment targets for capillary blood glucose levels:**
 - **fasting 90 to 99 mg/dl (5.0 to 5.5 mmol/l), 1 h after starting a meal <140 mg/dl (<7.8 mmol/l) or 2 h after starting a meal <120 to 127 mg/dl (<6.7 to 7.1 mmol/l).**

Managing DM in a pregnancy

- **The National Institute for Health and Clinical Excellence (NICE) recommendations for self testing in pregnancy are to have a fasting glucose between 3.5 and 5.9 mmol/l (63 and 106 mg/dl) and a 1-h postprandial glucose <7.8 mmol/l (<140 mg/dl)**
- **The updated Canadian Diabetes Association (CDA) guideline recommends plasma glucose target values during pregnancy as follows: fasting and preprandial 3.8 to 5.2 mmol/l; 1-h postprandial 5.5 to 7.7 mmol/l; 2-h postprandial 5.0 to 6.6 mmol/l**

Management of Gestational Diabetes

- **Strive to achieve glycemic targets**
- **Receive nutrition counselling from an Registered Dietitian**
- **Encourage physical activity**
- **Avoid ketosis**
- **If BG targets are not reached within 2 weeks then insulin therapy should be started**

GDM – Glycemic Targets

Recommended values for	Glycemic Targets
Pre-pregnancy Hb A1c	≤ 7.00 (if possible ≤ 6.00)
Pregnancy values	Range
FPG	70 - 95
1 hr PPG	100 - 140
2 hr PPG	90 - 120
Hb A1c	≤ 6.00

GDM and MNT

- **Two weeks trial of Medical Nutrition Therapy**
- **Pre-pregnancy BMI is a predictor of the efficacy**
- **If target glycemia is not achieved initiate insulin**
- **MNT – extra 300 calories in 2 and 3rd trimesters**
- **Calories – 30 kcal/kg/day = 1800 kcal for 60 kg**
- **If BMI > 30; then only 25 kcal/kg/day**
- **3 meals and 3 snacks – avoid hypoglycemia**
- **50% of total calories as CHO, 25% protein & fat**
- **Low glycemic, complex CHO, fiber rich foods**

Anti – diabetic drugs in Pregnancy

Drug Name	Pregnancy Category
Metformin	B
Pioglitazone	C
Glimepiride	C
Detemir	B
Glargine	C
Aspart/Lispro/RHI	B
Liraglutide	C
Sitagliptin	
Glulisine	C

Summary

- **Think Diabetes- Who to screen!**
- **Good History and Physical**
- **Educate, educate, educate!**
- **Monitor**
- **Be aggressive- don't be afraid to use insulin!**

Summary

- **Universal screening for glucose intolerance during pregnancy is essential as Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women.**
- **Asian women are ethnically more prone to develop glucose intolerance compared to other ethnic groups.**
- **GDM based on 2hr 75gm OGTT predicts adverse pregnancy outcome and warrants treatment.**
- **A 2 hr 75 gm post plasma glucose \geq 140mg/dl serves both as screening and diagnostic criteria besides being a simple and economical one step procedure.**
- **The timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition may prevent in all probability, India becoming diabetes capital of the World. As the routine**
- **screening for glucose intolerance during pregnancy is not**
- **done, probably the undiagnosed glucose intolerance that**
- **has been occurring in the past has resulted in the increased**
- **prevalence of diabetes in India.**
- **'No single period in human development provides a greater**
- **potential than pregnancy for long range pay off via relatively**
- **short range period of enlightened metabolic manipulation' -**
- **Norbert Fienkel.**

Presentation Outline

- **Epidemiology**
- **Classification**
- **Pathogenesis of glucose intolerance**
- **Consequences –Maternal/Fetal**
- **Screening & Diagnosis**
- **Management**

GDM: Definition

- Any degree of glucose intolerance with *onset or first* recognition during pregnancy, whether or not the condition persisted after pregnancy, and not excluding the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy.
- It has been related with at birth, intermediate and long term adverse effects; a common complication is macrosomia, which increases the risk for obstetric problems and birth injury, adult obesity and glucose intolerance in late adolescence and young adulthood.

Prevalence of DM

- Incidence continues to rise
- Global prevalence-2010, 6.4% adult population-171 million
- By 2030-7.8% - 438 million
- Varies from 10.2% in Western Pacific to 3.8% in African region - highest increase.
- 70% in low-& middle income countries.
- India is the world capital - 50.8 million, followed by China with 43.2 million.
- largest age group - 40-59 years.
- T2DM most common form with incidence of 85-95%.

The Burden

- **Approximately 7% of all pregnancies in the United States are complicated by gestational diabetes resulting in more than 200,000 cases annually.**
- **The prevalence ranges from 1% to 14% of all pregnancies depending on the population studied and the diagnostic tests used.**

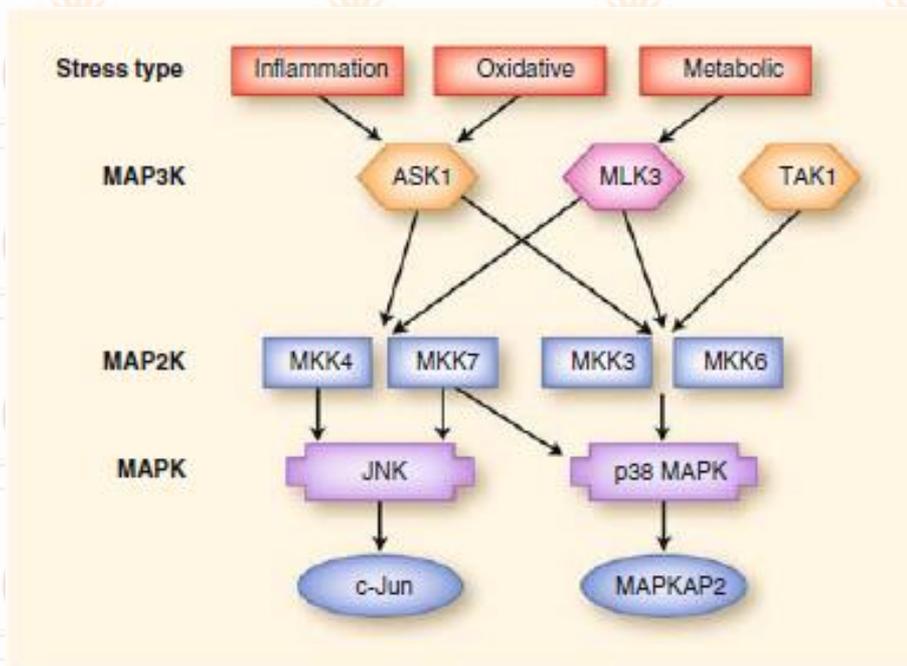
Gestational Diabetes Mellitus in India

- **An overall prevalence proportion of GDM at 17.7% in this rather young population of pregnant women was considerably high.**
- **Prevalence of 15% was obtained in another govt. hospital Chennai.**
- **15% in Trivandrum, 21% in Alwaye, 12% in Bangalore, 18.8% in Erode and 17.5% in Ludhiana.**
- **Recent national survey reported the prevalence of IGT in the age group of 20-29 years and 30-39 years as 12.2% and 15.3% respectively.**

Obesity and Pregnancy and IR

- Obesity has been proposed to impose a variety of stresses on adipose tissue, including inflammatory, metabolic, oxidative, and endoplasmic reticulum stress.
- Intra-abdominal fat contributes uniquely to the comorbidity of obesity compared with subcutaneous (SC) fat.
- In a recently published study, Bluher et al. (J Clin Endocrinol Metab 2009, 94:2507–2515) provided evidence of the ASK1-MKK4-p38 MAPK/JNK stress-sensing pathway in OM (omental) fat of obese patients that strongly associates with clinical markers of morbidity and predicts whole-body insulin sensitivity

Obesity and Pregnancy and IR



A study prospectively collected OM and abdominal SC fat samples from 20 women with normal pregnancies and nine GDM pregnancies during cesarean delivery.

Similar to obesity in nonpregnant women, the total expression of p38 MAP kinase was increased nearly twofold in OM compared with SC fat in GDM

Stress signaling in fat tissue by different stress sources. ASK—apoptosis signal-regulating kinase; JNK—c-Jun N-terminal kinase; MAP—mitogen-activated protein; MAPK—mitogen-activated protein kinase; MAPKAP2—mitogen-activated protein kinase-activated protein-2; MKK—mitogen-activated protein kinase kinase; MLK—mixedlineage kinase; TAK—transforming growth factor β -activated kinase

Adiponectin and GDM

- **Adiponectin is an adipocytokine that has been shown to have antiatherogenic, antiinflammatory, and antidiabetic roles. (Pajvani UB 2003)**
- **Chen et al 2006. found that the expression of adiponectin and its receptors is altered in women with GDM and suggested that adiponectin may play a role in adapting energy metabolism at the maternofetal interface.**
- **The involvement of adiponectin in insulin resistance during gestation was established by Cortelazzi et al.**
- **He found that Fetuses of diabetic mothers exhibited significantly lower adiponectin levels compared with normal fetuses of the same gestational age**

Resistin and GDM

- Resistin, a circulating cytokine, is produced in adipocytes and expressed abundantly in monocytes and macrophages.
- In animal experiments, resistin induces insulin resistance.
- Increased serum resistin levels were found in obesity, but controversy exists concerning its role in type 2 diabetes, insulin resistance, and hypertension in humans.
- According to these recent studies, resistin seems to play a rather **minor role** in the pathophysiology of GDM and the energy metabolism during fetal life.

GDM at risk

- **Pregnancy is associated with changes in insulin sensitivity which may lead to changes in plasma glucose levels.**
- **For women with known diabetes or for women who develop diabetes during the pregnancy, these changes can put outcomes at risk.**

Guidelines being revised

- **Since 2005 an evidence-based guideline on diabetes in pregnancy has been published in the UK** [National Collaborating

Centre for Women's and Children's Health. Diabetes in pregnancy. Revised reprint July 2008. London: RCOG Press. (www.nice.org.uk)]

- **The Canadian evidence-based diabetes guideline (including pregnancy) has been revised** [Can J Diabetes 2008; 32 (Suppl 1):

S168-S180]

- **There have been further deliberations on the implications of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study** [N Engl J Med 2008; 358: 1991-2002]

Problems with GDM

- **Maternal complications include:**
- **pre-eclampsia**
- **hyperglycemic crisis,**
- **urinary tract infections that may result in pyelonephritis,**
- **need for cesarean sections,**
- **morbidity from operative delivery,**
- **increased risk of developing overt diabetes,**
- **cardiovascular complications later in life, including hyperlipidemia and hypertension.**

Problems with GDM

- **Mothers with GDM have a 50% chance of developing type 2 diabetes mellitus (T2DM) for the 20 years following their diagnosis of GDM.**
- **Maternal hyperglycemia causes increased glucose delivery to the fetus, resulting in fetal hyperinsulinemia and increased fetal growth.**
- **Complications of excessive fetal growth include birth trauma, increased cesarean deliveries, and the long-term risk of glucose intolerance and obesity.**
- **Other immediate fetal complications include hypoglycemia, hyperbilirubinemia, respiratory distress syndrome, cardiomyopathy, and hypocalcemia**

GDM and Co-morbidities

- **Fourfold increased risk of hypertension during pregnancy.**
- **GDM with underlying preexisting moderate-to-severe nephropathy (urine albumin:creatinine ratio ≥ 300) or renal impairment (serum creatinine > 1.4 mg/dL) are at the greatest risk for deterioration**

GDM and Co-morbidities

- **High risk for PDR (retinopathy) at baseline—namely women with diabetes for greater than 10 years, pre-existing moderate-to-severe retinopathy, and poor glycemic control.**
- **Laser coagulation has been shown to be safe and efficacious in pregnancy for the treatment of the pre-proliferative stages of retinopathy.**
- **Prior retinopathy screening is a must**
- **Refractory to laser coagulation, termination of pregnancy can be considered given the high risk of permanent blindness**

GDM and Co-morbidities

- **Pre existing-Gastroparesis is considered a relative contraindication to pregnancy given the significant maternal morbidity and poor reported perinatal outcomes.**
- **Very difficult to manage as pregnancy itself causes the same**
- **Hydration, electrolyte imbalance and prokinetic agents may help**

GDM predisposes to CVD

CIRCULATION AHA.111.044784 Published online before print February 17, 2012, doi: 10.1161/

- **Women who experience pregnancy-related complications, particularly gestational diabetes and preeclampsia, are more likely to develop cardiovascular disease later in life.**
- **In the prospective Avon Longitudinal Study of Parents and Children (ALSPAC), researchers studied the associations of gestational diabetes, preeclampsia, preterm delivery and size for gestational age with calculated 10-year CVD risk and CV risk factors.**

According to study data, gestational diabetes and preeclampsia raised risk for CVD by 26% and 31%, respectively.

Researchers found gestational diabetes had a positive association with fasting glucose and insulin, whereas preeclampsia was associated with higher BMI, waist circumference, blood pressure, lipids and insulin.

The ORs for the calculated 10-year CVD risk based on the Framingham prediction score was 1.31 (95%

**ADA/EASD RECOMMENDATION
STANDARDS OF MEDICAL CARE
IN DIABETES—2013**

Recommendations: Detection & Diagnosis of GDM (1)

- Screen for undiagnosed T2D at the first prenatal visit in those *with risk* factors, using standard diagnostic criteria.
- In pregnant women not previously known to have diabetes, screen for GDM at 24–28 wks' gestation, using a 75-g OGTT & specific diagnostic cut points.
- Screen women with GDM for persistent diabetes at 6–12 wks' postpartum, using the OGTT & non-pregnancy diagnostic criteria.

Criteria for diagnosis of DM

A1C \geq 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

FPG \geq 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h plasma glucose \geq 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

Detection and Diagnosis of GDM (2)

- **Women with a history of GDM:**
 - **Should have lifelong screening for the development of diabetes or prediabetes at least every 3 years.**
 - **Found to have prediabetes should receive lifestyle interventions or metformin to prevent diabetes.**

Diagnosis of Gestational Diabetes

- **GDM carries risks for the mother & neonate.**
- **The HAPO study, demonstrated that risk of adverse maternal, fetal, & neonatal outcomes continuously increased as a function of maternal glycemia at 24-28 wks, even within ranges previously considered normal for pregnancy.**
- **IADPSG, recommended that all women not known to have prior diabetes undergo a 75-g OGTT at 24–28 wks of gestation.**

HAPO: Hyperglycemia & Adverse Pregnancy Outcomes

IADPSG: International Association of Diabetes & Pregnancy Study Groups

Screening for & Diagnosis of GDM

- Perform a 75-g OGTT, with BG measurement fasting & at 1 and 2 h, at 24–28 weeks' gestation in women not previously diagnosed with overt diabetes.
- Perform OGTT in the morning after an overnight fast of at least 8 h.
- GDM diagnosis: when any of the following plasma glucose values are exceeded
 - Fasting ≥ 92 mg/dL (5.1 mmol/L)
 - 1 h ≥ 180 mg/dL (10.0 mmol/L)
 - 2 h ≥ 153 mg/dL (8.5 mmol/L)

These new criteria will significantly increase the prevalence of GDM, primarily because only 1 abnormal value, not 2, is sufficient to make the diagnosis.

Diagnosing GDM

- **A definitive diagnosis of GDM is currently made on the result of an OGTT.**
- **Currently, a two-stage diagnostic procedure is conducted in some parts of the world.**
- **A two-stage procedure involves a non-fasting glucose challenge test (GCT) followed by a formal OGTT for women who have a positive result.**

GDM Screening at 24-28 weeks

1. Two-step approach:

- **A. Perform initial screening by measuring plasma or serum glucose 1 h after a 50-g oral glucose load.**
 - **A glucose threshold after 50-g load of 140 mg/dl identifies 80% of women with GDM, while the sensitivity is further increased to 90% by a threshold of 130 mg/dl.**
- **B. Perform a diagnostic 100-g OGTT on a separate day in women who exceed the chosen threshold on 50-g screening.**

~~2. One-step approach (may be preferred in clinics with high prevalence of GDM): Perform a diagnostic 100-g OGTT in all women to be tested at 24–28 weeks. The 100-g OGTT should be performed in the morning after an overnight fast of at least 8 h.~~

- **To make a diagnosis of GDM, at least two of the following plasma glucose values must be found:**
 - **Fasting: 95 mg/dl**
 - **1 h: 180 mg/dl**
 - **2 h: 155 mg/dl**
 - **3 h: 140 mg/dl**

100-g glucose load	mg/dl	mmol/l
Fasting	95	5.3
I-H	180	10
2-h	155	8.6
3-h	140	7.8
75-g glucose load		
Fasting	95	5.3
I-H	180	10
2-h	155	8.6

Diagnosis of GDM with a 100-g or 75-g glucose load

Questions

- **Does screening for & treating GDM affect infant or maternal morbidity or mortality?**
- **Does antepartum fetal testing prevent stillbirth or infant morbidity?**
- **Does postpartum glucose tolerance testing have an appreciable long term impact on women with a history of GDM?**

Question #1

**Does screening for & treating GDM
affect infant or maternal morbidity
or mortality?**

GDM Criteria

	National Diabetes Data Group*	American Diabetes Association*	World health Organization †	Carpenter and Coustan*
Fasting	105	92	≥ 126	95
1 hour	190	180	-	180
2 hours	165	153	≥ 140	155
3 hours	145	-	-	140

*2 or more criteria met = positive diagnosis (cutoff points in mg/dl)

† 1 or more criteria met = positive diagnosis

Screening & Diagnosis

- **Screen: 50g glucose 1 hour glucose challenge**
 - non-fasting state (higher or similar values with fast)
- **Diagnosis: 100g, 3 hour glucose tolerance test**
 - Positive test = 2 or more thresholds met/exceeded
 - No smoking prior
 - Unrestricted diet: at least 150g carbohydrates/d for at least 3 days prior (to avoid spurious high values)
 - One abnormal value with increased risk for macrosomic infants & associated morbidities

When to Screen?

- **24-28 weeks gestation**
- **Early screening:**
 - **marked obesity**
 - **personal history of GDM (33-50% likelihood recurrence)**
 - **glycosuria**
 - **strong family history of diabetes**

Maternal glucose
intolerance



Adverse pregnancy
outcomes

Recommendations

- **USPSTF:** “evidence is insufficient to recommend for or against routine screening.” (did find fair - good evidence that screening for GDM and treatment of hyperglycemia could reduce the frequency of fetal macrosomia)
- **ADA:** officially recommends screening for GDM, but may omit low risk women
- **ACOG:** universal screening is the most sensitive approach; screening may be omitted in low risk women, but universal screening as more practical approach

Treatment Questions

- **Does GDM pose serious risks to offspring?**
- **Does treatment reduce those risks?**
- **Does treatment reduce other risks associated with GDM (obesity/diabetes in offspring)?**
- **Does reducing glycemia reduce risks? (macrosomia & cesarean delivery)**

Risk Factors

- **Physical inactivity**
- **1st degree relative with diabetes**
- **Women who delivered a baby >9lbs +GDM**
- **Hypertension**
- **HDL<35 or Trigs >250**
- **Women with PCOS**
- **IGT or IFG on previous testing**
- **Hx CVD**
- **Severe obesity or acanthosis nigricans**
- **High risk ethnic groups(African-American, Latino, Asian-American, Pacific Islanders)**

Risk factors for GDM

- **Severe obesity**
- **Prior history of GDM or delivery of large-for-gestational-age infant**
- **Presence of glycosuria**
- **Diagnosis of PCOS**
- **Strong family history of type 2 diabetes**

Risk for GDM

Very High Risk

- Severe obesity
- Prior history of GDM or delivery of a large-for-gestation-age infant (>4,000 g/4,250 g/4,500 g)
- Presence of glycosuria
- Diagnosis of PCOS
- Strong family history of type 2 diabetes

Low Risk—Must Meet ALL of the Following Criteria:

- Age under 25
- Normal weight prior to pregnancy
- Member of an ethnic group with low prevalence of diabetes
- No known diabetes in first-degree relative
- No history of abnormal glucose tolerance
- No history of poor obstetrical outcomes

Average Risk—Criteria Not Met for High or Low Risk

Source: ADA 2009

Risk and Testing

- **Patients at very high risk for developing GDM should be screened as soon as pregnancy is confirmed using standard diagnostic testing.**
- **If this initial screening is negative, they are considered average risk and should be retested at 24 to 28 weeks of gestation using the one- or two-step approach.**
- **Women with average risk should be tested at 24 to 28 weeks of gestation.**
- **Those who meet all the criteria for low risk do not require testing**

Potential Risks

- **Macrosomia**
- **Brachial plexus injury**
- **Fracture with delivery**
- **Fetal hypoglycemia**
- **Fetal hyperbilirubinemia**
- **Fetal hypocalcemia**
- **Childhood obesity**
- **Neuropsychological outcomes**
- **Development of diabetes**
- **Perinatal mortality**
- **3rd/4th degree lacerations**
- **Instrument deliveries**
- **Cesarean delivery**
- **Preeclampsia**
- **Future diabetes mellitus**



Confounding Factors

- **Fetal size: maternal glucose levels, maternal BMI, pregnancy weight gain, parity**
- **Spectrum of sugars of normal to diabetic patients (single abnormal value of 3hGTT → large for gestational infants)**
- **Normal pregnancies with very narrow glucose range (euglycemia difficult to achieve)**
- **Alerting physicians to increased risk**

Treatment Approach

- Risk assessment at first PN visit
- Screen those at very high risk immediately
- Otherwise check at 24-28 weeks
- Initial check after 50g oral glucose load-
threshold of 130 or 140 THEN 100gm OGTT
on separate day in those who fail

PREDIABETES

- **Those patients with impaired fasting glucose(100-125) or IGT (2hr between 140-199)**
- **Both are risk factors for future DM and cardiovascular disease.**
- **Diet and Exercise.....how much?**
- **Follow up counseling important for success**
- **Metformin may be considered**

Physical Exam

- **Height, weight, BMI**
- **Blood pressure**
- **Fundoscopy exam**
- **Thyroid exam**
- **Skin-acanthosis nigricans**
- **Foot exam-inspection, pulses, reflexes, sensory**
- **Labs-HgbA₁C, liver, urine microalbumin, creatinine and GFR, TSH(DMI, inc lipids and women > 50)**

Management: Glycemic Control

- **Self monitoring of serum glucose**
- **3-4x/day DMI, less frequently in DMII or once daily insulin or oral meds**
- **Continuous glucose monitoring option**
- **Goal-HgbA₁C < 7% ADA, <6.5% ACE**
- **Pre-prandial 70-130mg/dl**
- **Peak Postprandial <180 gm/dl**

Medications-goals

- **Control sugar**
- **Control hypertension- goal <130/80**
- **Prevent/delay diabetic nephropathy-ACE^sARB^s**
 - albumin normal < 30
 - microalbuminuria 30-299
 - macroalbuminuria >300

Antiplatelet therapy

- **ASA-75-162mg/day *secondary* prevention w/ hx of CVD**
- **75-162mg/day *primary* prevention w/Type I and II w/ ↑CV risk, >40yo, hpt, smoking, dyslipidemia, albuminuria or FHx CVD**
- **Not recommended < 30 (no evidence to support)**
- **Combo therapy Plavix(clopidrogel) and ASA in pts with severe and progressive CVD**

Vaccinations

- **Flu shot annually**
- **Pneumovax for all adults with diabetes**
- **One time revaccination for ≥ 65 years of age if previously vaccinated < 65 and vaccine was administered > 5 yrs ago**
- **Absolutely no evidence or recommendation for more than 2 lifetime vaccinations**

Question #2

**Does antepartum fetal testing
prevent stillbirth or infant
morbidity?**

Antepartum Fetal Testing

- **Purpose: identify patients at risk for stillbirth**
- **Stillbirth rare occurrence**

■ **Pr** Insufficient evidence regarding
■ **AC** impact of antenatal fetal testing on
■ stillbirth rate, and neonatal
■ morbidity

- **NS/AF, tall biophysical profile**
- **No evidence regarding fetal ultrasound → macrosomia**

Question #3

Does postpartum glucose tolerance testing have an appreciable long term impact on women with a history of GDM?

Postpartum screening

- **50% women with GDM developing diabetes mellitus in a 28yr study (v. 7% of controls)**
- **Postpartum** No long-term follow-up studies that
- **6-8h** verify the benefit of postpartum
- **2h** diagnostic testing
- **Impaired: 140-199 (100-125)**
- **DM: ≥ 200 (≥ 126)**
- **Diet, exercise, weight reduction counseling**

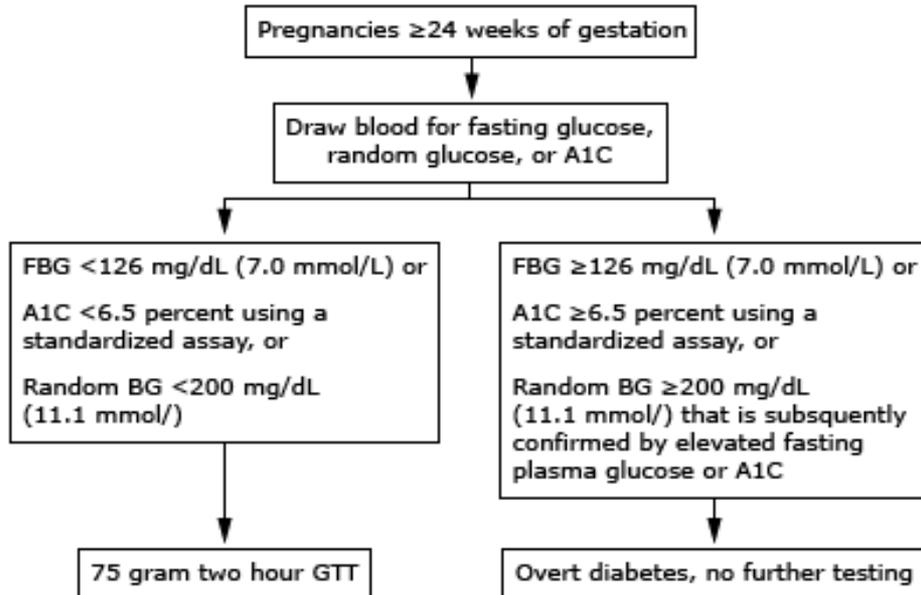
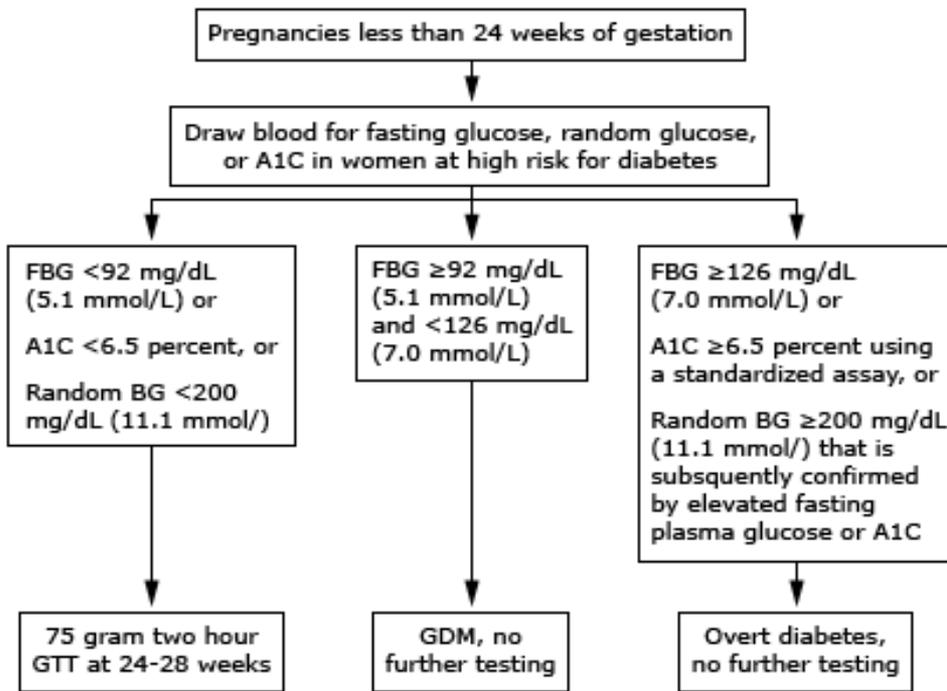
2011 UPDATE

- The IADPSG were created in 1998 to formulate recommendations for glucose tolerance testing in pregnancy.
- The IADPSG is made up of individuals from a variety of affiliated organizations with a focus on diabetes and pregnancy.
- The panel recommended the 2-h, 75-g OGTT for the diagnosis of GDM with the following thresholds

Time	Value + for GDM
<i>Fasting</i>	$\geq 92 \text{ mg}\%$ *
<i>1 hr</i>	$\geq 180 \text{ mg}\%$
<i>2 hr</i>	$\geq 153 \text{ mg}\%$

* After an 8 hour overnight fast

IADPSG



■ International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy.

■ Diabetes Care 2010; 33:676.

Criteria for a positive two hour 75 gram oral glucose tolerance test for the diagnosis of gestational diabetes

American Diabetes Association

At least two values that meet or exceed the following glucose concentrations:

Fasting	95 mg/dL (5.3 mmol/L)
One hour	180 mg/dL (10.0 mmol/L)
Two hour	155 mg/dL (8.6 mmol/L)

World Health Organization

Fasting	≥125 mg/dL (6.9 mmol/L)
OR	
Two hour	≥140 mg/dL (7.8 mmol/L)

International Association of Diabetes and Pregnancy Study Groups (IADPSG)

Fasting	≥92 mg/dL (5.1 mmol/L)
OR	
One hour	≥180 mg/dL (10.0 mmol/L)
OR	
Two hour	≥153 mg/dL (8.5 mmol/L)

These values represent the average glucose values at which infant birth weight, cord C-peptide, and percent body fat >90 percentile reached 1.75 times the estimated odds of these outcomes at mean glucose values from the HAPO study population, based on fully adjusted logistic regression models.

- No more 50 gm screening!
- No more 100 gm 3 hour GTT!
- Only one abnormal value
- Lower cutoffs for fasting and 2 hour



Fifth National Conference of Diabetes in Pregnancy Study Group, India

V Seshiah

5th – 7th Feb 2010, Kolkata

“Diabetes Free Generation - Focus on the Fetus for the Future”

“A single step procedure with a single glucose value” to diagnose abnormal glucose tolerance during pregnancy in the community - Indian Guidelines*

Representation from the National Bodies

Diabetes In Pregnancy Study Group India (DIPSI) - Dr V Seshiah, Dr A K Das, Dr V Balaji, Dr Sunil Gupta
Association of Physicians of India (API) - Dr B K Sahay, Dr Siddharth N Shah, Dr Debasis Maji, Dr Shashank R Joshi, Dr A Parneerselvam, Dr N Rajendran
Indian Medical Association (IMA) - Dr S Daga, Dr Samar Banerjee, Dr A Bhavatharani, Dr Madhuri S Balaji
Research Society for the Study of Diabetes In India (RSSDI) - Dr P V Rao, Dr HB Chandalia
Endocrinology Society of India - Dr A Ammini, Dr S K Sharma, Dr A H Zargar
Federation of Obstetrics and Gynecological Societies of India (FOGSI) - Dr H Konnar, Dr Sanjay Gupte, Dr Hema Divakar, Dr Sujata Misra, Dr Uday Thanawala, Dr Cynthia Alexander, Dr Ambarish Bhandiwad, Dr Anjalakshi C

1. Gestational Diabetes Mellitus (GDM)

1.1 Defining the condition and the aim of the declaration:

GDM is a clinical entity associated with a significant incidence of diabetes, in the later life of the mother and an increase in the fetal, neonatal morbidity and future development of obesity and diabetes in the offspring.^{1,2}

Pregnant women belonging to a high risk ethnic population (e.g. Indians) require *Universal Screening*. This observation emphasizes the need for an appropriate diagnostic tool to diagnose and method to treat GDM

criteria. Among them, the overall prevalence of GDM was 13.9%.⁵ Further, to ascertain the consistency of WHO criteria in diagnosing GDM, after determining the desired sample size with the required statistical power, a total of 1246 pregnant women underwent 75g OGTT. Among them 13.2% were detected to have GDM with a 2hr PG \geq 140 mg/dl. This finding substantiates and validates the previous prevalence data as well as the WHO criteria. Thus 2 hour plasma glucose \geq 140 mg with 75 gm oral glucose load has been accepted by the Diabetes in pregnancy Study group India (DIPSI) for diagnosing GDM (our population do not accept diagnosis based on FPG).

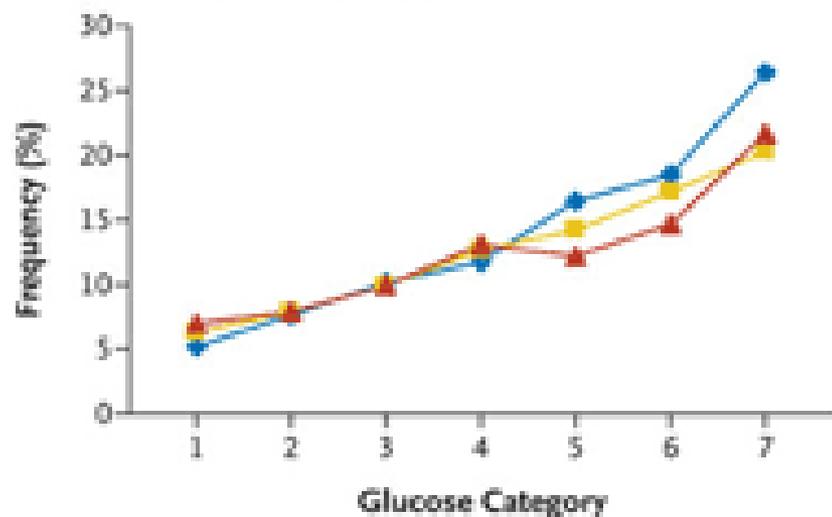
1.3 Short Term and Long Term Implications for the Progeny of GDM:

1.3.1 Increased birth weight of neonates was observed even when the mother's glucose tolerance was less than the glycemic criteria recommended by WHO for diagnosing GDM.⁶ The occurrence of macrosomia was continuum as the 2 hour plasma glucose with 75 gm OGTT, increased from 120 mg/ dl.^{7,8}

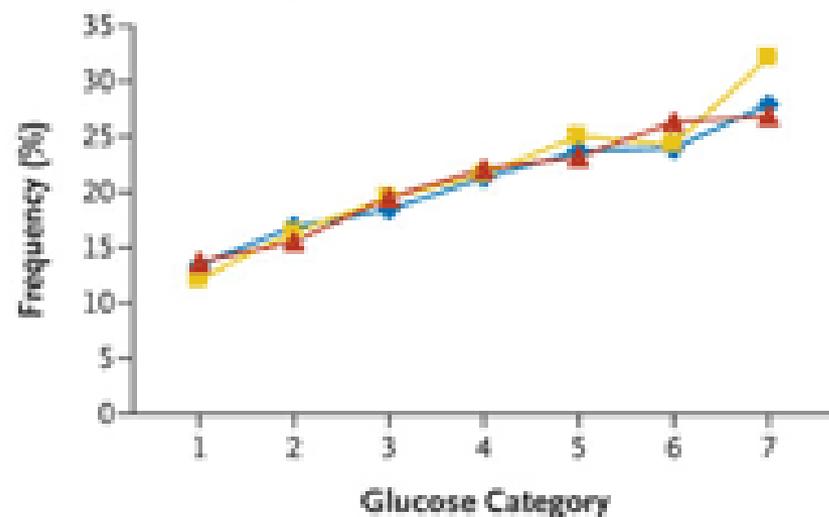
1.3.2 In children born to mothers who had third trimester plasma glucose 120 - 139 mg/ dl, the cumulative risk of developing type 2 diabetes was 19 % at age 24 years and this risk almost doubled to 30% with respect to those women who had 2 hour plasma glucose 140- 199 mg/ dl.⁹

◆ Fasting glucose
 ■ 1-Hr glucose
 ▲ 2-Hr glucose

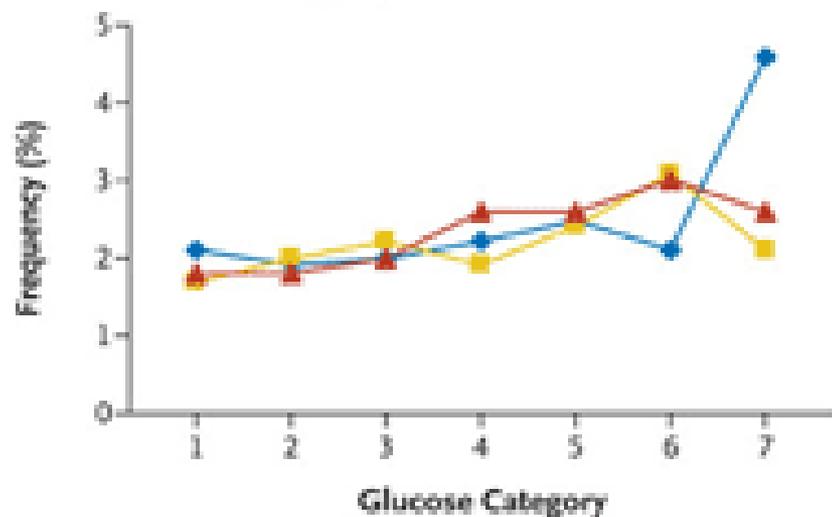
A Birth Weight >90th Percentile



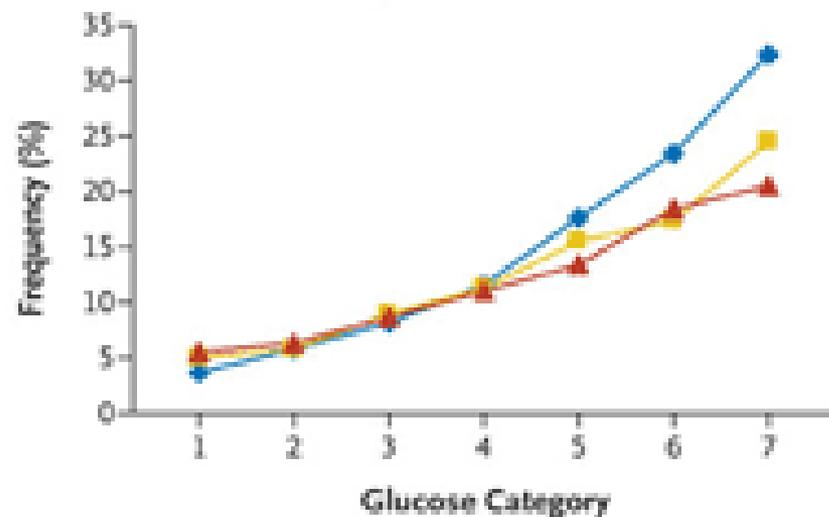
B Primary Cesarean Section

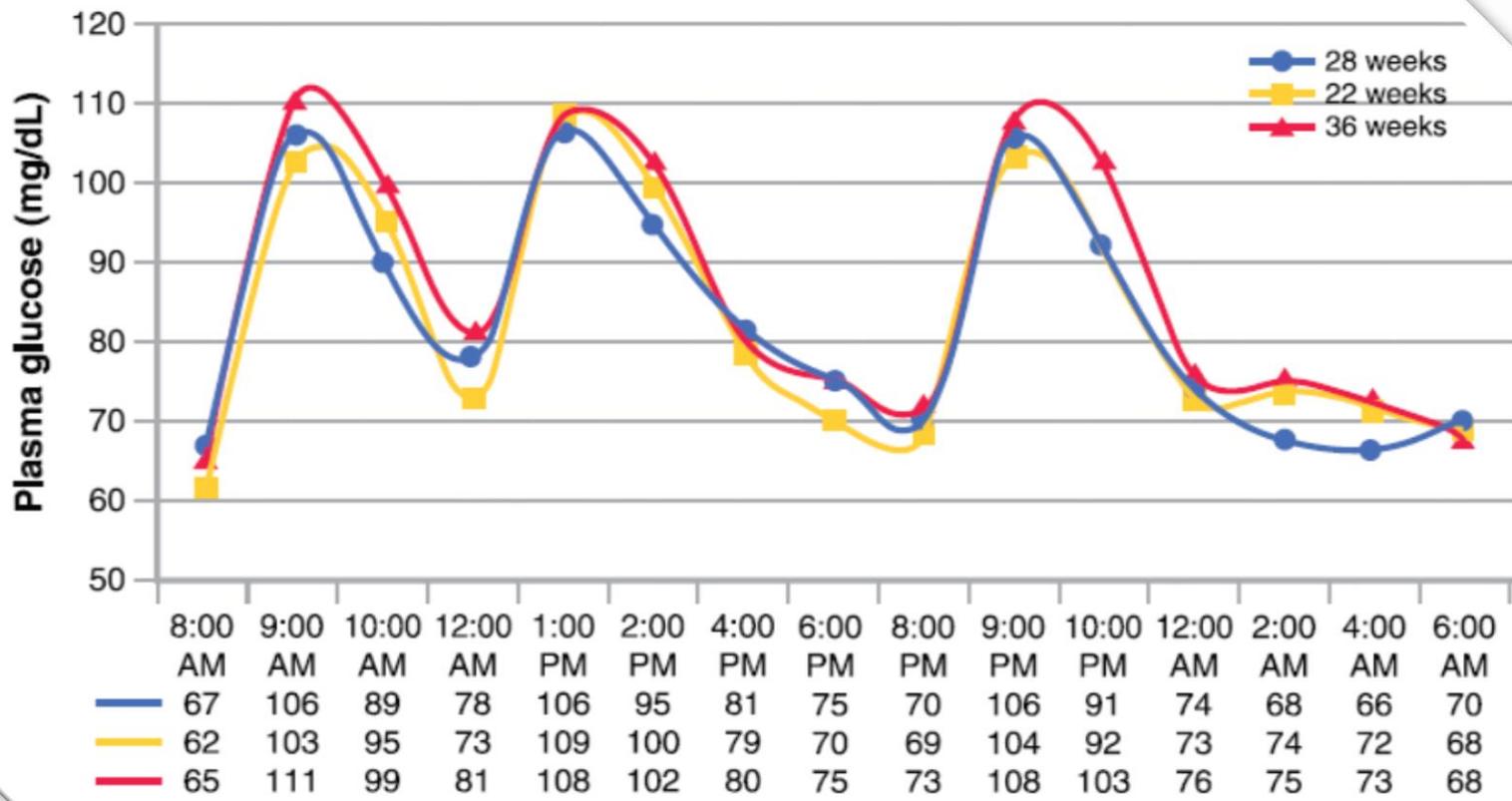


C Clinical Neonatal Hypoglycemia



D Cord-Blood Serum C Peptide >90th Percentile





Diurnal plasma glucose profile in normoglycemic third trimester gravidas. The numbers represent the 95th percentile values. (Adapted from Parretti E, Mecacci F, Panini M, et al.: Third trimester maternal glucose levels from diurnal profiles in nondiabetic pregnancies: Correlation with sonographic parameters of fetal growth. *Diabetes Care* 24:1317, 2001)

Overt DM in pregnancy

- In addition, the IADPSG also made recommendations regarding the diagnosis of overt diabetes during pregnancy.
- They recommended that
 - fasting plasma glucose (FPG) ≥ 126 mg/dL ,
 - a hemoglobin A1c (HbA1c; using a DCCT/ UKPDS standardized assay) $\geq 6.5\%$
 - random plasma glucose level ≥ 200 mg/dL (which requires confirmation by FPG or HbA1c) during the first trimester of pregnancy be diagnostic of overt diabetes.

Why treat GDM

- It is generally acknowledged that women with GDM are at increased risk of adverse pregnancy outcomes, particularly relating to perinatal mortality and morbidity
- Perinatal morbidity is an ongoing concern. Macrosomic or large-for-gestational-age (LGA) infants are still common, and can be considered a surrogate marker for at least some of the effects of intra-uterine programming.

Why treat GDM

- A prospective controlled trial demonstrated that ‘tight’ control, with a high rate of insulin use, improved perinatal outcomes [*Diabetes Care* 1988; 11: 761-8]
- Another prospective non-randomized intervention study demonstrated for women with GDM that intensive control (versus conventional control) improved perinatal outcomes to a level that was comparable to a group without GDM [*Am J Obstet Gynecol* 1994; 170: 1036-47]
- The Australian Carbohydrate Intolerance Study in Pregnancy (ACHOIS), a blinded randomized trial including 1000 women, designed to examine whether the treatment of women with GDM would reduce perinatal complications, found a significant reduction in serious perinatal complications in the treated group [*N Engl J Med* 2005; 352: 2477-86]
- Recently the results of the Maternal-Fetal Medicine Unit (MFMU) Network study have become available. Treating women with designated ‘mild’ GDM lowered the risk for many adverse pregnancy outcomes [*Am J Obstet Gynecol* 2009; 199(6) (Suppl A): S2]

Why treat GDM

- Limited observational studies in humans strongly suggest that any pregnancy complicated by hyperglycaemia confers a risk to the offspring of developing type 2 diabetes, and that improving maternal glycaemic control may reduce this risk.

[*Diabetes* 1988; 37: 622-8]

- However, the long follow-up necessary makes it unlikely that any randomized controlled trial (RCT) evidence will be forthcoming in the foreseeable future.

Recommendations

Before pregnancy

- **Particularly important for women who currently have diabetes or intermediate degrees of hyperglycaemia (impaired glucose tolerance – IGT, or impaired fasting glucose – IFG), or have experienced GDM in a previous pregnancy.**
- **The probability of developing GDM in a subsequent pregnancy is of the order of 30% to 50%. If more than a year has passed since the postpartum assessment, then these women should have an oral glucose tolerance test (OGTT) prior to conception or at least in the first trimester.** [Diabetes Care 2007; 30: 1314-9]
- **If the glycaemic status is then normal, the OGTT should be repeated at around 26 to 28 weeks, or at an earlier time if clinically indicated.**

Diabetic control before conception

- **Spontaneous miscarriages appears to be low when the HbA1c is modestly raised, and higher with increasingly poor glycaemic control** [Am J Obstet Gynecol 1987; 156: 1096-100]
- **The same pattern is also found with respect to the rate of fetal malformations.** [Teratology 1989; 39: 225-31]
- **Women with diabetes should be encouraged to obtain the best possible glycaemic control before conception, an HbA1c <6.5% (or <7.0% if on insulin).**
- **Some consensus opinions advocate a lower value and this is reasonable if it can be safely achieved and maintained.**

Managing DM in a pregnancy

- **Whenever it is possible, pregnant women with diabetes should be encouraged to self-monitor blood glucose levels both fasting and postprandial, preferably 1 h after a meal.**
- **The target glucose levels should be as low as possible compatible with patient comfort and safety.**
- **The conclusions of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus, in the absence of specific evidence, referred to ‘upper boundary’ treatment targets for capillary blood glucose levels:**
 - **fasting 90 to 99 mg/dl (5.0 to 5.5 mmol/l), 1 h after starting a meal <140 mg/dl (<7.8 mmol/l) or 2 h after starting a meal <120 to 127 mg/dl (<6.7 to 7.1 mmol/l).**

Managing DM in a pregnancy

- **The National Institute for Health and Clinical Excellence (NICE) recommendations for self testing in pregnancy are to have a fasting glucose between 3.5 and 5.9 mmol/l (63 and 106 mg/dl) and a 1-h postprandial glucose <7.8 mmol/l (<140 mg/dl)**
- **The updated Canadian Diabetes Association (CDA) guideline recommends plasma glucose target values during pregnancy as follows: fasting and preprandial 3.8 to 5.2 mmol/l; 1-h postprandial 5.5 to 7.7 mmol/l; 2-h postprandial 5.0 to 6.6 mmol/l**

Insulin in pregnancy

- **For the long-acting insulin analogues, there is limited experience in pregnancy.**
- **Recently insulin detemir has been FDA approved for use in pregnancy, and a large met analysis also showed that Glargine is safe, however awaits approval.**
- **The decision about which type of insulin and which insulin regimen to start or continue during pregnancy should be taken after informed discussion.**
- **The more limited clinical experience and therefore the theoretical possibility of as yet unknown risks associated with the newer insulin analogues needs to be balanced against patient preference and overall glycaemic control and stability.**

Glargine in pregnancy-Meta analysis

- **OBJECTIVE:** To determine the fetal safety of insulin glargine use in the treatment of diabetes in pregnancy compared with NPH insulin therapy.
- **METHODS:** A systematic review and meta-analysis was performed of all original human studies that reported neonatal outcomes among women with pregestational or gestational diabetes who were managed with either insulin glargine or NPH insulin during pregnancy.
 - A systematic literature search was conducted using MEDLINE, EMBASE, CINAHL, the Cochrane Central Register for Controlled Trials database, and Web of Science from 1980 to June 1, 2010.
- **RESULTS:** Eight studies reporting on a total of 702 women with pregestational or gestational diabetes in pregnancy treated with either insulin glargine (n = 331) or NPH insulin (n = 371) met the inclusion criteria.
 - There were no statistically significant differences in the occurrence of fetal outcomes studied with the use of insulin glargine compared to NPH insulin.

CONCLUSIONS: No evidence has been documented for increased adverse fetal outcomes with the use of insulin glargine in pregnancy compared to the use of NPH insulin.

Insulin Glargine Safety in Pregnancy

A transplacental transfer study

Diabetes Care Jan 2010

OBJECTIVE of this study was to determine whether insulin glargine crosses the human placenta using the human perfused placental lobule technique.

RESEARCH DESIGN AND METHODS

Insulin glargine, at a therapeutic concentration of 150 pmol/l (20 μ U/ml) was added to the maternal circulation.

Additional experiments were carried out at concentrations 1,000-fold higher than therapeutic levels (150, 225, and 300 nmol/l).

The appearance of insulin glargine in the fetal circulation was analyzed by a chemiluminescence immunoassay.

RESULTS

Results from perfusions carried out at therapeutic concentrations (150 pmol/l) of insulin glargine showed no detectable insulin glargine in the fetal circuit.

After perfusion with very high insulin glargine concentrations of 150, 225, and 300 nmol/l, the rate of transfer remained low

Anti – diabetic drugs in Pregnancy

Drug Name	Pregnancy Category
Metformin	B
Pioglitazone	C
Glimepiride	C
Detemir	B
Glargine	C
Aspart/Lispro/RHI	B
Liraglutide	C
Sitagliptin	
Glulisine	C

Summary

- **Think Diabetes- Who to screen!**
- **Good History and Physical**
- **Educate, educate, educate!**
- **Monitor**
- **Be aggressive- don't be afraid to use insulin!**

Summary

- **Universal screening for glucose intolerance during pregnancy is essential as Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women.**
- **Asian women are ethnically more prone to develop glucose intolerance compared to other ethnic groups.**
- **GDM based on 2hr 75gm OGTT predicts adverse pregnancy outcome and warrants treatment.**
- **A 2 hr 75 gm post plasma glucose ≥ 140 mg/dl serves both as screening and diagnostic criteria besides being a simple and economical one step procedure.**
- **The timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition may prevent in all probability, India becoming diabetes capital of the World.**

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Thank you

Pathophysiology

Pregnancy is Diabetogenic condition
A Wonderful Metabolic Stress Test

Insulin resistance due to placental secretion of anti-insulin hormones

Progesterone, Cortisol, GH

Human Placental Lactogen (HPL), Prolactin

Late pregnancy:

- Maternal hepatic glucose production increases by 15%-30% to meet fetal demand¹

- Beta-cell dysfunction

Gestational diabetes mellitus (GDM)

Pancreatic beta-cell dysfunction caused by:

- Genetics
- Autoimmune disorders

Risk Factors: for first trimester screening

- ≥ 35 yrs
- BMI ≥ 30
- Previous GDM/ Delivery of a macrosomic baby
- Member of a high-risk population (eg. South Asian, Asian)
- PCOS
- Glucosuria
- Strong family h/o T2DM

Criteria for a positive two hour 75 gram oral glucose tolerance test for the diagnosis of gestational diabetes

American Diabetes Association

At least two values that meet or exceed the following glucose concentrations:

Fasting	95 mg/dL (5.3 mmol/L)
One hour	180 mg/dL (10.0 mmol/L)
Two hour	155 mg/dL (8.6 mmol/L)

World Health Organization

Fasting	≥125 mg/dL (6.9 mmol/L)
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OR

Two hour	≥140 mg/dL (7.8 mmol/L)
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International Association of Diabetes and Pregnancy Study Groups (IADPSG)

Fasting	≥92 mg/dL (5.1 mmol/L)
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OR

One hour	≥180 mg/dL (10.0 mmol/L)
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OR

Two hour	≥153 mg/dL (8.5 mmol/L)
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These values represent the average glucose values at which infant birth weight, cord C-peptide, and percent body fat >90 percentile reached 1.75 times the estimated odds of these outcomes at mean glucose values from the HAPO study population, based on fully adjusted logistic regression models.

SCREENING

- Only one abnormal value
- Lower cutoffs for fasting and 2 hour

2011 UPDATE

- The IADPSG were created in 1998 to formulate recommendations for glucose tolerance testing in pregnancy.
- The IADPSG is made up of individuals from a variety of affiliated organizations with a focus on diabetes and pregnancy.
- The panel recommended the 2-h, 75-g OGTT for the diagnosis of GDM with the following thresholds

Time	Value + for GDM
<i>Fasting</i>	$\geq 92 \text{ mg}\%$ *
<i>1 hr</i>	$\geq 180 \text{ mg}\%$
<i>2 hr</i>	$\geq 153 \text{ mg}\%$

* After an 8 hour overnight fast



DIPSI Guidelines - Kolkata Declaration

Fifth National Conference of Diabetes in Pregnancy Study Group, India

V Seshiah

5th – 7th Feb 2010, Kolkata

“Diabetes Free Generation - Focus on the Fetus for the Future”

“A single step procedure with a single glucose value” to diagnose abnormal glucose tolerance during pregnancy in the community - Indian Guidelines*

Representation from the National Bodies

Diabetes In Pregnancy Study Group India (DIPSI) - Dr V Seshiah, Dr A K Das, Dr V Balaji, Dr Sunil Gupta
Association of Physicians of India (API) - Dr B K Sahay, Dr Siddharth N Shah, Dr Debasis Maji, Dr Shashank R Joshi, Dr A Parneerselvam, Dr N Rajendran
Indian Medical Association (IMA) - Dr S Daga, Dr Samar Banerjee, Dr A Bhavatharani, Dr Madhuri S Balaji
Research Society for the Study of Diabetes In India (RSSDI) - Dr P V Rao, Dr HB Chandalia
Endocrinology Society of India - Dr A Ammini, Dr S K Sharma, Dr A H Zargar
Federation of Obstetrics and Gynecological Societies of India (FOGSI) - Dr H Konnar, Dr Sanjay Gupte, Dr Hema Divakar, Dr Sujata Misra, Dr Uday Thanawala, Dr Cynthia Alexander, Dr Ambarish Bhandiwad, Dr Anjalakshi C

1. Gestational Diabetes Mellitus (GDM)

1.1 Defining the condition and the aim of the declaration:

GDM is a clinical entity associated with a significant incidence of diabetes, in the later life of the mother and an increase in the fetal, neonatal morbidity and future development of obesity and diabetes in the offspring.^{1,2}

Pregnant women belonging to a high risk ethnic

criteria. Among them, the overall prevalence of GDM was 13.9%.⁵ Further, to ascertain the consistency of WHO criteria in diagnosing GDM after determining the desired sample size with the required statistical power, a total of 124 pregnant women underwent 75g OGTT. Among them 13.2% were detected to have GDM with 2hr PG \geq 140 mg/dl. This finding substantiates and validates the previous prevalence data as well as the WHO criteria. Thus 2 hour plasma glucose \geq 140 mg with 75 gm oral glucose load has been accepted by the Diabetes in pregnancy Study group India (DIPSI) for diagnosing GDM (our population do not accept diagnosis based on FPG).

1.3 Short Term and Long Term Implications for the Progeny of GDM:

1.3.1 Increased birth weight of neonates was observed even when the mother's glucose tolerance was less than the glycemic criteria recommended by WHO for diagnosing GDM.⁶ The occurrence of macrosomia was continuum as the 2 hour plasma glucose with 75 gm OGTT, increased from 12 mg/ dl.^{7,8}

1.3.2 In children born to mothers who had third trimester plasma glucose 120 - 139 mg/ dl, the cumulative risk of developing type 2 diabetes was

Patient (and Partner) Education

Compliance depends on the patient's understanding

- **Implications of GDM for her baby and herself**
- **Diet/ safe physical activity**
- **Self monitoring of blood glucose**
- **Self administration /adjustment of insulin**
- **Hypoglycemia**
- **Techniques to reduce stress and cope with denial**