Universal Screening and Timely Intervention in Gestational Diabetes Mellitus: A Key to Successful Feto-Maternal Outcome

DR PRASANTA KUMAR NAYAK
Assistant professor, Department of OBGYN
AIIMS
AGENDA

• Recommendations for universal screening of GDM
• Recommendations for time of screening of GDM
• What happens if GDM is not treated?
• Effect of GDM on mother
• Effect of GDM on fetus
• Effect of treatment of GDM cases
GESTATIONAL DIABETES MELLITUS

Glucose intolerance of variable severity with onset or first recognition during pregnancy
GDM REDEFINED...

Overt / pre-gestational diabetes - Diagnosis of hyperglycemia in the first trimester as per non-pregnant cut-offs

GDM - Diagnosis of hyperglycemia in the 2nd or 3rd trimester

WHO-2013: Hyperglycemia in pregnancy
FBS≥126 mg/dl and PGBS≥200 mg/dl : Diabetes in pregnancy (It is any time during pregnancy)

Diabetes Care Volume 37, Supplement 1, January 2014
Endocrine Society 2013
Diabetes doesn’t discriminate.
WHAT ABOUT GDM

• Whether it affects only high risk category women
  ➢ BMI>25 kg/m²
  ➢ Physical inactivity
  ➢ First degree relative with DM
  ➢ High risk ethnicity (Asian American, Latino, African American etc)
  ➢ Delivery of baby weighing >9 lb or H/O GDM
  ➢ HTN, CVD, PCOD
  ➢ HDL<35 mg/dl or TGs>250 mg/dl

• It can affect any one irrespective of the risk factors
EVEN TODAY THE WORLD DIVIDES ON THE FOLLOWING ASPECTS OF GDM

- Universal screening or risk based screening?
- Time of screening: (First trimester and/or At 24-28 weeks of gestation)
WHOM TO SCREEN?

Universal screening
- ADA 2014
- WHO 2013
- ES 2013
- IADPSG 2010
- DIPS1 2006

RISK BASED SCREENING
- ACOG 2001
- NIH 2013
WHEN TO SCREEN

• The fetal beta cells recognise maternal serum glycemic level as early as 16\textsuperscript{th} week of gestation.


• The peak of insulin resistance is observed between 24\textsuperscript{th} to 28\textsuperscript{th} week of gestation.
## WHEN TO SCREEN

<table>
<thead>
<tr>
<th>GESTATIONAL AGE</th>
<th>IADPSG / ADA</th>
<th>DIPSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester or 1st antenatal visit</td>
<td>Screen for type-2 DM in high risk group only with 75gm OGTT and interpret as non-pregnant OGTT values</td>
<td>Screen for GDM universally</td>
</tr>
<tr>
<td>24-28 weeks</td>
<td>Screen for GDM</td>
<td>Screen for GDM if previous test normal</td>
</tr>
<tr>
<td>32-34 weeks</td>
<td>---------------------------</td>
<td>Screen for GDM if previous test normal</td>
</tr>
</tbody>
</table>
WHY THIS HUE AND CRY?
ITS BECAUSE OF TWO THINGS

• Very high prevalence of GDM

• Significant adverse feto-maternal outcome
**PREVALENCE OF GDM- GLOBAL**

- Global prevalence: 16.8% (21.4 million)

<table>
<thead>
<tr>
<th>IDF REGION</th>
<th>Cases in live births</th>
<th>Prevalence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>4.6</td>
<td>14.4</td>
</tr>
<tr>
<td>EUR</td>
<td>1.7</td>
<td>12.6</td>
</tr>
<tr>
<td>MENA</td>
<td>3.4</td>
<td>17.5</td>
</tr>
<tr>
<td>NAC</td>
<td>0.9</td>
<td>10.4</td>
</tr>
<tr>
<td>SACA</td>
<td>0.9</td>
<td>11.4</td>
</tr>
<tr>
<td>SEA</td>
<td>6.3</td>
<td>25.0</td>
</tr>
<tr>
<td>WP</td>
<td>3.7</td>
<td>11.9</td>
</tr>
</tbody>
</table>

*Comparative prevalence

IDF diabetes atlas-2013
META-ANALYSIS FINDING OF VARIABLE PREVALENCE OF GDM ACROSS STUDIES AND DIAGNOSTIC CRITERIA

<table>
<thead>
<tr>
<th>Hartling L et al</th>
<th>Review Methods</th>
<th>Prevalence of GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The search identified 14,398 citations and included 97 studies (6 randomized controlled trials, 63 prospective cohort studies, and 28 retrospective cohort studies) between 1995 to May 2012</td>
<td>ADA(75gm): 2 to 19%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carpenter&amp; Coustan: 3.6 to 38%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDDG: 1.4 to 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WHO: 2 to 24.5%</td>
</tr>
</tbody>
</table>

INCREASING PREVALENCE – WHY?

- Change in life style
- Increasing prevalence of obesity & type 2 DM
- More women with pregnancy at advanced age
- More detection rate due to improved health care
- Lower cut offs for diagnosis and universal screening
IF GDM IS NOT TREATED
## META-ANALYSIS TO SHOW OUTCOMES OF NON-TREATED GDM

<table>
<thead>
<tr>
<th>Hartling L et al</th>
<th>REVIEW METHODS</th>
<th>RESULTS</th>
<th>CONCLUSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thirty-eight studies examined health outcomes for women who met different criteria for GDM and did not undergo treatment</td>
<td>Methodologically strong studies showed a continuous positive relationship between increasing glucose levels and the incidence of primary CS and macrosomia. One study also found significantly fewer cases of preeclampsia, CS, shoulder dystocia and/or birth injury, clinical neonatal hypoglycemia, and hyperbilirubinemia for women without GDM compared with those meeting IADPSG criteria</td>
<td>Evidence supports a positive association with increasing plasma glucose on a 75 g/100 g OGTT and macrosomia and primary CS, clear thresholds for increased risk were not found</td>
<td></td>
</tr>
</tbody>
</table>

EFFECTS OF GDM ON MOTHER

PERIPARTUM
• Pre-eclampsia
• Polyhydramnios
• Preterm labour
• Operative delivery

LONG TERM
• Type 2 DM
• CVD
• Metabolic syndrome
EFFECTS OF GDM ON FETUS

PERINATAL

- Macrosomia
- IUGR
- Organomegaly
- Shoulder dystocia
- Birth trauma
- RDS
- Hypoglycemia
- Hyperbilirubinemia
- Abortion or sudden IUFD

LONG TERM

- Obesity
- Type-II DM
- CVD
- Impaired cognitive development
- Impaired motor function
GDM & ITS LEGACY - VICIOUS CYCLE

- Maternal Hyperglycemia
- Fetal Hyperinsulinemia
- Increased Fetal Fat Cells
- Childhood Obesity and Insulin Resistance
- Impaired Glucose Tolerance and Diabetes in Adulthood
## WHETHER ADVERSE PREGNANCY OUTCOMES IN GDM IS INDEPENDENT OF OTHER RISK FACTORS?

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NUMBER OF PATIENTS</th>
<th>STUDY OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metzger et al (HAPO study)</td>
<td>25505</td>
<td>GDM complications are independent of other confounding factors (Age, BMI, Mean BP, Parity, smoking, Height, Family Hist)</td>
</tr>
<tr>
<td>Sermer M et al</td>
<td>4274</td>
<td>Increasing maternal carbohydrate intolerance associated with a graded increase in adverse maternal and fetal outcome</td>
</tr>
<tr>
<td>Schmidt MI et al</td>
<td>4977</td>
<td>GDM predicts adverse pregnancy outcomes</td>
</tr>
<tr>
<td>Sacks DA et al</td>
<td>3505</td>
<td>Positive association between maternal blood glucose and birth weight percentiles</td>
</tr>
</tbody>
</table>

EVIDENCE TO SHOW ADVERSE EFFECTS OF GDM ON MOTHER
## Evidence to Show GDM as a Risk Factor for Preeclampsia

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Study Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmidt MI et al</td>
<td>4977</td>
<td>GDM associated with adverse pregnancy outcomes including preeclampsia</td>
</tr>
<tr>
<td>Metzer BE et al</td>
<td>25505</td>
<td>Among the secondary outcomes strongest associations was found for preeclampsia</td>
</tr>
</tbody>
</table>


# EVIDENCE TO SHOW GDM AS A RISK FACTOR FOR CAESAREAN DELIVERY

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NO. OF PATIENTS</th>
<th>STUDY OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugaya A et al</td>
<td>416</td>
<td>GDM significantly increased caesarean section rate</td>
</tr>
<tr>
<td>Metzer BE et al</td>
<td>25505</td>
<td>Significant increase in caesarean section rate as a primary outcome</td>
</tr>
<tr>
<td>Aberg A et al</td>
<td>4526</td>
<td>Significant increase in caesarean delivery among women with a glucose tolerance value between 140-162 mg/dl</td>
</tr>
</tbody>
</table>


The study by Moses et al and the HAPO study showed a dose-response gradient across maternal glucose levels for the various adverse pregnancy outcomes.

HIGHLIGHTS OF ADVERSE MATERNAL OUTCOME IN FUTURE

- 30-84% chances of recurrence; most significantly influenced by race with higher risk in nonwhite race/ethnicity
- 7-fold increased risk of developing type 2 DM in future
- Increased risk for cardiovascular diseases & metabolic syndrome

SYSTEMATIC REVIEW TO FIND THE PREDICTORS OF FUTURE TYPE-II DM AMONG GDM MOTHERS

<table>
<thead>
<tr>
<th>STUDY</th>
<th>RESULT</th>
<th>CONCLUSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Golden SH et al(2009)</td>
<td>5 out of 11 studies showed that FBG, in the antepartum OGTT is a significant predictor of future T2DM (odds ratio [OR] range: 11.1-21.0; relative risk [RR] range: 1.37-1.5; relative hazard [RH] = 2.47). Risk of incident T2DM was predicted by the antepartum 2-hour OGTT plasma glucose in 3 studies (OR range: 1.02-1.03; RR = 1.3) and by the antepartum OGTT glucose AUC in 3 other studies (OR range: 3.64-15; RH = 2.13).</td>
<td>FBG, OGTT 2-hour blood glucose, and OGTT glucose AUC appeared to be strong and consistent predictors of subsequent T2DM among women who met diagnostic criteria for GDM using the OGTT</td>
</tr>
</tbody>
</table>

GDM AS A CAUSE OF CARDIOVASCULAR DISEASES IN MOTHER

• Pre-eclampsia is a novel cardiovascular risk marker.

• Pre-eclampsia increases both the long term risk of cardiovascular disease and the risk that it will occur earlier.


<table>
<thead>
<tr>
<th>Bellamy L et al</th>
<th>Review methods</th>
<th>RESULTS</th>
<th>CONCLUSIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prospective and retrospective cohort studies were included, providing a dataset of 3,488,160 women, with 198,252 affected by pre-eclampsia (exposure group) and 29,495 episodes of cardiovascular disease and cancer (study outcomes)</td>
<td>The RR (95% CI) for HTN were 3.70 (2.70 to 5.05) after 14.1 yrs weighted mean follow-up, for IHD 2.16 (1.86 to 2.52) after 11.7 years, for stroke 1.81 (1.45 to 2.27) after 10.4 years, and for VTE 1.79 (1.37 to 2.33) after 4.7 years. No increase in risk of any cancer was found (0.96, 0.73 to 1.27), including breast cancer (1.04, 0.78 to 1.39) 17 years after pre-eclampsia</td>
<td>A history of PE should be considered when evaluating risk of CVD in women. This association might reflect a common cause for PE and CVD, or an effect of PE on disease development, or both. No association was found between PE and future cancer</td>
</tr>
</tbody>
</table>

ADVERSE EFFECTS OF GDM ON FETUS
INTRA UTERINE FETAL PROGRAMMING

Gestational programming is a process whereby stimuli or stresses that occur at critical or sensitive periods of fetal development, permanently change structure, physiology, and metabolism, which predispose individuals to disease in adult life.

GESTATIONAL PROGRAMMING AND FUTURE DIABETES MELLITUS

- Epigenetic regulation of gene expression: Through this mechanism, genetic susceptibility and environmental insults can lead to Type-II DM
- T2D is a disorder of complex genetics influenced by interactions between susceptible genetic loci and environmental perturbations such as IUGR.
- An abnormal metabolic intrauterine milieu affects fetal development by permanently modifying expression of key genes regulating β-cell development (Pdx1) and glucose transport (Glut4) in muscle

GESTATIONAL PROGRAMMING AND OTHER HEALTH DISORDERS OF OFFSPRINGS IN FUTURE

• Poor health in utero leads to poor pregnancy outcomes, which in turn lead to poor health in childhood(1)

• Young children with poor health are, in turn, at higher risk for serious conditions in adulthood such as obesity and cardiovascular disease (1)

• Altered placental perfusion, may contribute to the development of long term adverse outcomes in the offspring(2)


## EVIDENCE TO SHOW ASSOCIATION OF MACROSOMIA IN GDM

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NO. OF PATIENTS</th>
<th>STUDY OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aberg A et al</td>
<td>4526</td>
<td>Macrosomia associated with GDM</td>
</tr>
<tr>
<td>Black MH et al (Retrospective study)</td>
<td>9835</td>
<td>Overweight and GDM together leads to LGA babies</td>
</tr>
<tr>
<td>Wendland EM et al (Review article)</td>
<td>44829</td>
<td>GDM consistently associated with macrosomia and LGA babies when WHO diagnostic criteria was used</td>
</tr>
</tbody>
</table>


# EVIDENCE TO SHOW GDM AND PERINATAL MORTALITY AND MORBIDITY

<table>
<thead>
<tr>
<th>Study</th>
<th>No of Patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wendland EM et al (cohort)</td>
<td>4401</td>
<td>In settings of limited detection and treatment of gestational diabetes mellitus, women across a spectrum of lesser than diabetes hyperglycemia, experienced a continuous rise in perinatal death with increasing levels of glycemia after 34 weeks of pregnancy</td>
</tr>
<tr>
<td>Dodd JM et al (cohort)</td>
<td>16975</td>
<td>With increasing plasma glucose values, there is a significant increase in shoulder dystocia and neonatal hypoglycemia</td>
</tr>
<tr>
<td>Nayak PK et al (cohort)</td>
<td>304</td>
<td>NICU admission of neonates of GDM mothers were significantly higher</td>
</tr>
</tbody>
</table>

GDM AND LONG TERM FETO-MATERNAL ADVERSE OUTCOME

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Result of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’ Sullivan JB et al</td>
<td>615</td>
<td>Only one trial showing no association of future diabetes even 16 years after GDM.</td>
</tr>
<tr>
<td>Gillman MW et al</td>
<td>199</td>
<td>Treatment of mild GDM did not affect BMI at age 4-5 years</td>
</tr>
</tbody>
</table>

There is lack of data to show long-term effects of GDM treatment on offspring morbidity and to show the effect of treatment on the improvement of maternal outcomes in later life.

Predictors for antenatal insulin requirement in gestational diabetes

Subarna Mitra\(^1\), Prasanta Kumar Nayak\(^1\), Jayaprakash Sahoo\(^2\), Agnes Mathew\(^3\), Alaganandam Padma\(^3\), Sadishkumar Kamalanathan\(^2\), and Sarita Agrawal\(^1\)

\(^1\)Department of Obstetrics & Gynecology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India, \(^2\)Department of Endocrinology & Metabolism, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, and \(^3\)Department of Obstetrics & Gynecology, Pondicherry Institute of Medical Sciences, Puducherry, India

Abstract
The purpose of this study was to identify pre-gestational and gestational factors predicting subsequent insulin requirement in patients with gestational diabetes mellitus (GDM). Maternal parameters were compared between mothers achieving glycemic control with or without the addition of antenatal insulin therapy (AIT). Insulin was required only in 8/83 (10%) patients for glycemic control. Those who needed insulin had a stronger family history of diabetes and higher first hour plasma glucose along with multiple (>1) abnormal values during oral glucose tolerance test (OGTT) in univariate analysis (p < 0.05). The first hour plasma glucose value of \(\geq 9.72\) mmol/l predicted requirement of AIT in GDM mothers with a sensitivity of 100% and specificity of 73%. However, only positive family history of diabetes mellitus among first degree relatives and multiple abnormal values in OGTT were independent predictors for antenatal insulin requirement in regression analysis.

Keywords
Body mass index, gestational diabetes, insulin

History
Received 13 November 2013
Revised 13 March 2014
Accepted 31 March 2014
Published online 14 May 2014
CAN TREATMENT FOR GDM REDUCE ADVERSE PREGNANCY OUTCOMES

<table>
<thead>
<tr>
<th>STUDY</th>
<th>RCT(Int.GP/Control GP)</th>
<th>EFFECTS OF TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACHOIS TRIAL Crowther CA et al</td>
<td>490/510</td>
<td>Rate of serious perinatal complications (Perinatal mortality, shoulder dystocia, birth trauma etc) reduced and so also macrosomia, LGA and hypertensive disorders</td>
</tr>
<tr>
<td>Landon MB et al</td>
<td>485/473</td>
<td>Treatment of mild GDM reduces the risks of LGA, Shoulder dystocia, caesarean delivery and hypertensive disorders</td>
</tr>
<tr>
<td>Falavigna et al</td>
<td>Systematic review with 7 studies</td>
<td>Treatment of GDM significantly reduced the risk of macrosomia, LGA, shoulder dystocia (allocation concealment was clearly specified in above two studies)</td>
</tr>
</tbody>
</table>

DIAGNOSING AND TREATING GESTATIONAL DIABETES PROVIDES

“An opportunity to prevent feto-maternal complications during pregnancy and after pregnancy”