Changing trends in the management of gestational diabetes mellitus

Chandrika N Wijeyaratne
Dept of Obstetrics & Gynaecology
University of Colombo
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Mrs SL
36 years G3P1C1 POA 8 weeks

FBS = 110 and 2h PPBS = 168 mg/dl
Patient denies she has diabetes

II\textsuperscript{ry} subfertility
P1 (2003) – LSCS B Wt 3.9kg
G2 (2012) - miscarriage 14 weeks
Current pregnancy – LMP unknown (irregular periods)
BMI 35 kg/m\textsuperscript{2} BP 140/100 mmHg
ODQ – worked 4 years in the Middle East
Weight gained >10kg
Ix for subfertility upon her return to SL in 2011

Case notes of subfertility clinic (2012)
OGTT 0h - 140
   1h - 280  mg/dl
   2h - 220

HbA1C = 8.6%
TSH 2.58, U/S – no dominant follicle

NO INTERVENTION FOR HER METABOLIC CONTROL
The management of anovulatory infertility in women with polycystic ovary syndrome: an analysis of the evidence to support the development of global WHO guidance

Adam H. Balen¹*, Lara C. Morley¹, Marie Misso², Stephen Franks³, Richard S. Legro⁴, Chandrika N. Wijeyaratne⁵, Elisabet Stener-Victorin⁶, Bart C.J.M. Fauser⁷, Robert J. Norman⁸, and Helena Teede²

¹Leeds Centre for Reproductive Medicine, Leeds Teaching Hospitals, Leeds LS1 46UH, UK ²Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash University, Monash Medical Centre, 43–51 Kanooka Grove, Clayton VIC 3168, Australia ³Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash University, Monash Medical Centre, Clayton VIC 3168, Australia ⁴Center for Reproductive Medicine, University of Pennsylvania Perelman School of Medicine, Pennsylvania, U.S.A. ⁵Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology, Brigham and Women’s Hospital, Boston, Massachusetts, U.S.A. ⁶Department of Obstetrics and Gynecology, University of California, San Francisco, California, U.S.A. ⁷Department of Obstetrics and Gynecology, University of California, San Francisco, California, U.S.A. ⁸Department of Obstetrics and Gynecology, University of California, San Francisco, California, U.S.A.
The female life cycle

- Fetus
- Infant
- Pre-pubertal child
- Adolescent
- Pregnancy & childbirth
- Reproductive years
- Menopause
- Post-menopause

Genes
- IU environment
- Infancy
- Pre-pubertal child
- Adolescence
- Adult
- Obesity
- Anovulation

HRT
- CVD events
- Reproductive years
- Further wt gain
- MetS, CAD risks
- Fertility Rx
- GDM, PIH, IUGR

Catch up growth
FEMALE GENDER: THE KEY TO DIABETES PREVENTION?

– Lise Kingo

It starts with a healthy pregnancy

- Low birth weight
- Large for gestational age birth weight

In adult life
- Elevated risk for:
  - Obesity
  - Diabetes
  - Hypertension
  - CVD

Intergenerational transfer of risk

Maternal health – The link to the NCD epidemic

Adapted from: The Female Gender: The Key to Diabetes Prevention: presented by Lise Kingo at the 6th International Symposium on Diabetes & Pregnancy. Mar 23-26, 2011, Salzburg Austria
Diabetes in pregnancy in South Asia (2012)

- Policy makers and planners must prioritize the amalgamation of MCH and Diabetes prevention programmes at national level.

- Adopt a life cycle approach to the problem across generations.
- capacity building – from field service to tertiary care
- develop a cost effective evidence based approach
- include screening for DM to Pre Conception Care Package
Avoid an unplanned pregnancy – the essential component of diabetes education for women

Adopt prevention from adolescence

Women with diabetes be offered professional support for pre-pregnancy assessment
“Hyperglycemia is common with one out of six live births leading to maternal and neonatal morbidity, and an increased risk of future obesity, diabetes and CVD of mother and child”

“relevance as a priority for maternal health and impact on the future burden of NCD ..... needs a greater global action plan focused on preventing, screening, diagnosing and managing HIP – from the adolescent, to preconception and maternal nutrition guidelines .......”

Moshe Hod, Chair of the Expert Group for the FIGO GDM Initiative
Hyperglycaemia in pregnancy

Pre-existing diabetes (DIP)
- Type1
- Type2

Gestational diabetes
- Pre-existing diabetes
- True GDM
## Risks of diabetes in pregnancy

<table>
<thead>
<tr>
<th>Pre-existing diabetes</th>
<th>Gestational</th>
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<tbody>
<tr>
<td>Miscarriage</td>
<td>Neonatal hypoglycaemia</td>
</tr>
<tr>
<td>Congenital malformation</td>
<td>Perinatal death</td>
</tr>
<tr>
<td>Stillbirth</td>
<td></td>
</tr>
<tr>
<td>Neonatal death</td>
<td></td>
</tr>
</tbody>
</table>

- **fetal macrosomia**
- **birth trauma (to mother and baby)**
- **induction of labour or caesarean section**
- **transient neonatal morbidity**
- **obesity and/or diabetes developing later in the baby’s life**
Diabetes in Pregnancy – (Pre-gestational)

Type 1 and type 2 diabetes confer graver maternal and fetal risk than GDM

Should be ideally managed pre-conception

If not IMMEDIATELY upon detection
Screening
Evidence

• Insufficient to advocate universal screening ....noting maternal hyperglycaemia caused adverse fetal outcomes.....

• Insulin improved pregnancy outcomes viz. perinatal outcomes - death, macrosomia, shoulder dystocia, nerve palsy and fracture were significantly reduced.

2002 NICE - UK

2005 ACHOIS

The Maternal Fetal Medicines Unit (MFMU) Network trial favouring universal screening - but acknowledged considerable controversy.

2007, Landon

• Biochemical screening for women with risk factors

2008, NICE guideline

Risk factor based vs Universal screening - likely to miss 30-60% of GDM
A continuum of risk across for adverse perinatal outcomes

EVEN LOWER maternal glucose levels

Figure 1. Frequency of Primary Outcomes across the Glucose Categories.
New evidence clearly demonstrates that

• There is a continuous linear relationship between maternal glucose and fetal growth

• Fetal growth can be modified by glucose-lowering therapies, with diet and lifestyle intervention often being successful


Screening & diagnosis

Much confusion

Different options (>20 yrs)

Different diagnostic tests and cut off values

- DIPSI guidelines: non-fasting 75-g glucose challenge test (GCT)
- WHO 1999 criteria: (FPG and 2h value)
- 3 point fasting 75g OGGT:
  HAPO/WHO 2013 criteria
3 point fasting 75g OGTT: WHO 1999 criteria & HAPO/WHO 2013 criteria

- Confusion on cut off value
- WHO (1999)- based on future risk of T2DM
IDPASG

- Recommends - one-step 75 g oral glucose tolerance test for **all women not already known to be diabetic** at 24–28 weeks POA

- Diabetes is diagnosed where **one or more** threshold value is exceeded

  - Fasting $\geq 5.1$ mmol/l = 92 mg/dL
  - 1-hour $\geq 10.0$ mmol/l = 180 mg/dL
  - 2-hour $\geq 8.5$ mmol/l = 153 mg/dL

1.75 x the mean for HAPO study population
DIPSI guidelines: non-fasting 75g glucose challenge test (GCT)

- Convenient
- Single sample
- No fasting
- Single value
Timing

- Mid trimester (24-28w) GDM screening-sorted!
- Universal screening
- What about first trimester?
• >95% Sri Lankan women ANC booking before 8 weeks gestation

• Studies have demonstrated high prevalence of first trimester hyperglycaemia in Sri Lanka

• Majority of women with T2DM/IGT are unaware of their glycaemic status preconception
• Establishing good blood glucose control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death.

• Detection may also allow interventions targeting at reduction of PET, IUGR, macrosomia and related complications.
Booking visit and early detection of “hyperglycaemia” in pregnancy

- Detecting pre-existing, unrecognized diabetes
- Allows implementation of “effective” intervention packages
  - Screening for nephropathy, retinopathy - lower risk of PIH/PET/IUGR
  - Aspirin
  - High dose folate
  - High risk pathway for fetal monitoring - Structural anomalies/ UAD
  - Earlier and better control of glycaemia
NICE Recommends

• a 75 g 2-hour OGTT as soon as possible after booking (whether in the first or second trimester) and

• a further 75 g 2-hour OGTT at 24–28 weeks if the results of the first OGTT are normal

(even earlier for high risk women)
Guideline for screening, diagnosis and management of diabetes in pregnant women in Sri Lanka recommends:

a. One stage, non-fasting 75g OGTT as described by the Diabetes in Pregnancy Study group of India (DIPSI)

b. Three point 75g oral GTT

c. 2 hour Post Prandial Blood Glucose Testing (PPBS) when glucose loading not feasible

Screening using fasting blood glucose, random blood glucose, 50g glucose challenge test, HBAIC or urinalysis for reducing substances is not recommended

FHB, July 2013
One stage Non-fasting OGCT

- all pregnant women to be screened at the 1st visit and at 24-28 weeks.
- 2-hour blood glucose more than 140mg/dl confirms gestational diabetes.
- Recommended test for both field and institutional levels.
- Advantage the most convenient for universal screening, low cost, make a diagnosis in one test and not requiring to fast. Validated against the WHO and HAPO criteria.
1st Trimester screening in 5 MOH areas

<table>
<thead>
<tr>
<th>Screening Area</th>
<th>Total number of 1st Trimester mothers screened</th>
<th>Positive &gt;140(%)</th>
</tr>
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<tbody>
<tr>
<td>Pitakotte</td>
<td>203</td>
<td>73 (35.9%)</td>
</tr>
<tr>
<td>Hanwella</td>
<td>396</td>
<td>78 (19.6%)</td>
</tr>
<tr>
<td>Piliyandala</td>
<td>595</td>
<td>111 (18.6%)</td>
</tr>
<tr>
<td>Padukka</td>
<td>380</td>
<td>78 (20.5%)</td>
</tr>
<tr>
<td>Kaduwela</td>
<td>424</td>
<td>135 (31.8%)</td>
</tr>
</tbody>
</table>
Summary - screening

- “Universal screening” at “booking visit”
- National Guideline recommendation
- GCT or PPBS for convenience
- Detecting preexisting DM or IGT priority
- FBS unsuitable in pregnancy
- HbA1c ?
Managing
GDM
Increased risk of T2DM for mother
Increased risk of obesity and type 2 diabetes in offspring later in life

DIP / GDM postpartum - Discuss family planning
• Prescribe effective contraception

Women with preexisting type 1 or type 2 diabetes
• Counsel on the risk of fetal development
• If HbA1C ≥8% defer pregnancy
• Exclude end organ effects viz., Nephropathy (IUGR/ PET)
• Assess risk for diabetic retinopathy
Eye exams before pregnancy/ 1st trimester; monitor every trimester and for 1 year postpartum
GDM risks of complications
- increased with progressive hyperglycemia
- reduced with diet, physical activity, and lifestyle counseling

Lifestyle management
- Medical nutrition, physical activity, weight management

Pharmacologic therapy
- Insulin is first line
- Requires frequent titration to match changing requirements
- Most insulins are category B
  - Glargine, glulisine, and degludec are category C

Metformin - appropriate for high BMI
Specialist decision recommended
Insulin is the preferred medication for DIP-type 1 and type 2 diabetes not adequately controlled with diet, exercise and metformin

Insulin during pregnancy
- Requires frequent titration to match changing requirements
- Referral to specialized center recommended

Women with T1D are at high risk for hypoglycemia
- Hypoglycemia education - before and during pregnancy

Women with T1D are at risk for ketoacidosis
- Provide education on prevention and treatment of DKA

Women with type 2 diabetes are at risk for obesity
- Recommended weight gain during pregnancy: 6-11 kg overweight, 4.5-9 kg lb obese
- Glycemic control easier to achieve but may require higher insulin doses
Modification of Medication

- **Type 1 diabetes**
  - Discontinue long acting analogue (glargine) and substitute with NPH/detemir

- **Type 2 diabetes**
  - Discontinue all OADs (except metformin)
  - Discontinue long acting analogue (glargine) and substitute with NPH/detemir

**Medications to be discontinued** - ACEi, Statins

- Consider low dose Aspirin
- Do a retinal assessment
Individualized counseling
Basic plan - based on recommendations for all pregnant women
Adjust to individual needs
Dietary advice

CHO and caloric contents - modified based on the height, weight, and degree of glucose intolerance

Caloric restriction - 33% reduction results in clinically relevant improvement in glycemic parameters

- 30-35 kcal/kg/day = 1500 Kcal/d is safe
- 50% -complex carbs
- Exact amount unknown - based on individual needs, mother’s weight, activity, home & personal circumstances
- Base on home blood glucose levels
Specific targets

- Avoid concentrated sweets and highly processed foods

Some more tips

- Breakfast be especially small and low in carbs because insulin resistance is highest in the morning
- High-fiber and low-GI foods substituted for simple sugars (legumes, oats, parboiled rice)
- Assist in delaying absorption of food to match insulin peak
- Foods rich in antioxidants? role in reducing the incidence of fetal anomalies
- Fruits and vegetables – warn re quantities!

Hone J. J Clin Endocrinol Metab 2010
Physical activity

• Sustains insulin sensitivity & improves glucose clearance
• Decreases TNF-α originating from the placenta which directly correlates with the level of insulin resistance throughout pregnancy
• A 10-minute activity session timed at 30 minutes after each meal may help to control post-meal glucose excursions and reduce the need for insulin

<table>
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<th>Glycemic Targets in Pregnancy</th>
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<tr>
<td>Pre-pregnancy diabetes (DIP)</td>
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<tr>
<td>Gestational diabetes mellitus (GDM)</td>
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**Fasting**
- ≤90 mg/dL (5.0 mmol/L)  
- ≤95 mg/dL (5.3 mmol/L)

**1-hr Postprandial**
- ≤130 - 140 mg/dL (7.2 - 7.8 mmol/L)  
- ≤140 mg/dL (7.8 mmol/L)

**2-hr Postprandial**
- ≤120 mg/dL (6.7 mmol/L)  
- ≤120 mg/dL (6.7 mmol/L)

**HbA1C%**
- 6.0-6.5% (42-48 mmol/L) recommended  
- < 6% optimal with progression of pregnancy

**Achieve without hypoglycaemia**

**GDM-**

Postprandial normoglycemia can reduce the rate of fetal macrosomia

HAPO, 2008
Why these tight glycemic targets?

Prospective study in type1 patients with pregnancy

<table>
<thead>
<tr>
<th>FBS</th>
<th>Macrosomia</th>
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<tbody>
<tr>
<td>&gt;105 mg/dl</td>
<td>28.6 %</td>
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<tr>
<td>95-105</td>
<td>10%</td>
</tr>
<tr>
<td>&lt;95 mg/dl</td>
<td>3%</td>
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Blood glucose monitoring

- 4 times/day minimum - fasting and 1 to 2 hours after start of meals
- Maintain log book
- Use a memory meter
- Calibrate the glucometer frequently
• Initial clinic attendance - for patient education
• Subsequently - SMBG
• Long-term control - 4-6 weekly HbA1c

Glycaemic control shown to be improved by limiting postprandial glucose excursions
• Postprandial glucose correlates well with HbA1C
• By measuring and controlling the postprandial and fasting sugars, the occurrence of neonatal hypoglycaemia and macrosomia reduced

de Veciana M. NEJM 2013
When to initiate medication therapy

• When BGs are greater than 20% beyond target despite meal plan and exercise adherence:
  – Three or more elevated fasting BGs and/or
  – Six or more post meal elevations in 1 week

• Before starting insulin evaluate for:
  – Persistent FBG >90 mg/dL (three or more in 1 week)

• Degree of elevation above the target values: mild to moderate
  – Fasting BG 90–120 mg/dL, post meals 130–180 mg/dL
  – Estimated LGA fetus >90th percentile or abdominal circumference >70th percentile on ultrasound

(Buchanan et al, 2007)
Insulin

- When to start insulin?
- If PG/BG values exceed

**SMBG every 3\(^{rd}\) day**
- Review every 3\(^{rd}\) day
- Insulin dose change accordingly

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<tbody>
<tr>
<td>1-h postprandial PG</td>
<td>≥155</td>
<td>8.6</td>
</tr>
<tr>
<td>2-h postprandial whole BG</td>
<td>≥120</td>
<td>6.7</td>
</tr>
<tr>
<td>2-h postprandial PG</td>
<td>≥130</td>
<td>7.2</td>
</tr>
</tbody>
</table>
Insulin regimen - MDI versus CSII (p > 0.05)

Calculate total daily dose requirement
Start with small doses
Teach insulin self injection technique and supervise
Pre-mix insulin twice daily 30/70 or 50/50– preferred
Give 2/3 dose in the morning
Lunch may need “cover” with short acting insulin or metformin
Avoid night hypos

Alternative basal bolus regime  (Analogue preferred)

MDI regimen preferred
under medical supervision and MD team support
Sulfonylureas:
• Inferior to insulin and metformin due to increased risk of neonatal hypoglycemia and macrosomia
• No long-term safety data

Metformin - starting dose 500 mg once daily & increasing to 500 mg tds
• Similar outcomes between metformin and insulin
• 46% required additional insulin
• Early indicator that metformin therapy alone is inadequate is a higher fasting glucose

• Dosage should be increased every 4-5 days
• Cross the placenta - no reports of fetal effects
• Long term effects under study - optimism of safety
• Decreased maternal weight gain

Targets - are we pitching too low?

Techniques of assessment
• SMBG & HbA1c

Target values in pregnancy - derived from pregnant T1DM & T2DM patients

- FPG of \( \leq 5.0 \) mmol/L - Associated with reduced risk of macrosomia, neonatal hypoglycemia, and maternal preeclampsia in 3\(^{rd}\) trimester
  - Prutsky et al. JCEM 2013

- FPG \( \leq 4.9 \) mmol/L and 2hPPBG 5.9–6.4 mmol/L
  Risk of macrosomia, prematurity, neonatal hypoglycaemia & preeclampsia all lowered
  - Rowan et al. Diab Care 2010
Myths & Misconceptions

• a pregnant woman needs to eat for two
• a pregnant woman must eat unlimited *polos, kos, del* etc
• sugared food and drink is nourishing and will produce good breast milk
• advertisements of Anmum, Mama Sustagen and Enfamum say my baby will be healthy and brainy
• exercise in pregnancy is not good
• will my baby get diabetes?
• taking insulin is harmful to my baby
• a big baby is a healthy baby
Myths & Misconceptions and Cultural issues

- Urine testing is sufficient
- My family members had a “little sugar” in the past or got only when “old”
- Will my husband’s family make differential Rx
- My husband says I cannot ‘guard my mouth’
- I do not want to waste food leftover by my other kids
- I cannot cook my food separately
- Will breast feeding pass on excess sugar to my baby?
- This will all go away after pregnancy
- I do not need family planning
**SUMMARY**

**HbA1C** - Type 1 DM, maintain ~6% before and <6% during pregnancy

**Behavioural change** - team effort and commitment and sensitivity to patient needs with shared care

**Regular BSS** – ideally SMBG (if not office based)

Remember - capillary whole BG vs Plasma glucose

**Targets** – Pre meal, bedtime, overnight (3.3-5.4 mmol/L)
  
  Postprandial 5.4-6.7 mmol/L

Avoid night hypos

**Monitoring – combined effort**

- Regular BSS- mainstay of optimization of metabolic control
- 3-4 times a day
- pre-breakfast and PPBS(-lunch and dinner) and bed time

**Long term metabolic follow up** – breastfeeding & FP
Mrs SL
36 years G3P1C1 POA 8 weeks

FBS = 110 and 2h PPBS = 168 mg/dl
Patient denies she has diabetes

EARLY RECOGNITION AND PRE-EMPTIVE ACTION THROUGH MULTI-DISCIPLINARY APPROACH

BMI 35 kg/m²  BP 140/100 mmHg
Colombo Declaration is ‘just the beginning’

South Asian leaders have pledged to make the link between maternal health and diabetes a public health priority. It’s a promising step in a growing global effort, advocates for healthier pregnancies say.