GWG: maternal and fetal components

GWG and interventions

- Diet and/or physical activity
- 36 RCTs, 12,526 women
- Mean reduction – 0.7 kgs overall
- No difference in obese women
- No improvement in pregnancy outcomes

(Khan et al. BMJ, 2017)

REPEAT WEIGHING

- Stressful
- Stigmatisation
- Small-for-gestational-age with <5 kgs weight gain?
- Suboptimal nutrients?
Learning points

- Evidence basis for IOM GWG recommendations poor
- Obese women have lower GWG without interventions
- Definition of “excessive” GWG in obese women inequitable
- Benefits and risks of measuring GWG unproven

III. Maternal obesity and Gestational Diabetes Mellitus

ORs for GDM (2000-6)

<table>
<thead>
<tr>
<th>Category</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight</td>
<td>2.1</td>
</tr>
<tr>
<td>Obese</td>
<td>3.6</td>
</tr>
<tr>
<td>Severely Obese</td>
<td>8.6</td>
</tr>
</tbody>
</table>

(GDM rate 1-20%; 20 studies)

(Chu et al. 2007)
### Adverse pregnancy outcomes (FPG)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW &gt; 90th centile (n=2221)</td>
<td>1.39</td>
<td>1.32 – 1.44</td>
</tr>
<tr>
<td>Primary CS (n=3731)</td>
<td>1.11</td>
<td>1.06 – 1.15</td>
</tr>
<tr>
<td>Cord C-peptide (n=480)</td>
<td>1.55</td>
<td>1.47 – 1.64</td>
</tr>
<tr>
<td>Neonatal hypoglycemia (n=48)</td>
<td>1.08</td>
<td>0.98 – 1.19</td>
</tr>
</tbody>
</table>

(HAPO, 2008)
Response to HAPO

- Meeting convened by IADPSG
- 220 delegates, writing subgroup established
- New criteria for GDM proposed
- OR 1.75 compared with mean glucose
- One increased value only
- 2-hour 75g one-step OGTT

Carpenter Coustan
100g OGTT

<table>
<thead>
<tr>
<th>Timing</th>
<th>Level (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>5.3</td>
</tr>
<tr>
<td>1-hour</td>
<td>10.0</td>
</tr>
<tr>
<td>2-hour</td>
<td>8.6</td>
</tr>
<tr>
<td>3-hour</td>
<td>7.8</td>
</tr>
</tbody>
</table>

> One values

IADPSG
75g OGTT

<table>
<thead>
<tr>
<th>Timing</th>
<th>Level (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>5.1</td>
</tr>
<tr>
<td>1-hour</td>
<td>10.0</td>
</tr>
<tr>
<td>2-hour</td>
<td>8.5</td>
</tr>
</tbody>
</table>

Only one value

Incidence of GDM (HAPO)

- Overt diabetes 1.8%
- Post-hoc GDM 16.1%
- Total 17.9%
HAPO diagnostic criteria

- Endorsed by IADPSG
- Endorsed initially by American Diabetes Association
- Endorsed by WHO (in the interests of consensus)
- Not endorsed by ACOG
- Not endorsed by US Preventive Taskforce 2013
- Not endorsed by Canada

HAPO diagnostic criteria

- Endorsed in Ireland 2010
- Partially endorsed by European Board (EBCOG) 2015
- Not endorsed by UK (NICE)

GDM (Coombe)

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>GITs</td>
<td>679</td>
<td>1375</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>GDM</td>
<td>139</td>
<td>221</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.02</td>
<td>p&lt;0.02</td>
</tr>
</tbody>
</table>

GDM rates in 19 units (2008)

(Source: HIPE 2007-18, NPRS 2008-13, IMIS 2014-17)

GDM in 19 units, Ireland (2008-17)

(Source: HIPE 2008-17, NPRS 2008-13, IMIS 2014-17)

GDM rates in 19 maternity units (2017)

(Source: HIPE 2008-17, NPRS 2008-13, IMIS 2014-17)
Rates of GDM in 4 largest units

(Sources: HIPE 2008-17, NPRS 2008-13, IMIS 2014-17)

GDM rates USA

Learning points

- Implementation of HAPO diagnostic criteria increased GDM rates dramatically in Ireland
- Implementation highly variable nationally
- Benefits and risks of new criteria uncertain
Maternal obesity and exercise RCT

- Intensive, supervised exercise intervention
- Primary end-point: decreased maternal glucose
- FPG decreased by 0.4 mmol/l at OGTT
- Secondary end-point: decreased GWG

Conclusions

1. Excessive GWG in obese women decreased from 45% to 24% (p<0.05) but difference not sustained
2. Exercise did not improve maternal glycaemic control or decrease incidence of GDM
3. Research samples higher glucose measurements than customary samples
Laboratory standards

1. Pre-analytical
2. Analytical
3. Post-analytical

Preanalytical glycolysis

- Plasma not blood glucose
- Process of glycolysis long established
- 5-7% per hour
- Need inhibition after phlebotomy
- Immediate centrifugation
Venous blood collected into bottles containing fluoride EDTA

Laboratory analysis: Hexokinase method

Methods: paired sample handling

Venous blood collected into bottles containing fluoride EDTA

Customary Conditions

Research Conditions

Room temperature

On iced slurry

To laboratory in clusters

To laboratory immediately

Laboratory analysis Hexokinase method
Mean phlebotomy to laboratory (mins) at 24-28 week OGTT (n=24 pairs)

<table>
<thead>
<tr>
<th></th>
<th>Customary</th>
<th>Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose</td>
<td>166 ± 33</td>
<td>27 ± 17</td>
</tr>
<tr>
<td>1-hour glucose</td>
<td>105 ± 26</td>
<td>23 ± 16</td>
</tr>
<tr>
<td>2-hour glucose</td>
<td>45 ± 26</td>
<td>25 ± 40</td>
</tr>
</tbody>
</table>

(Daly et al, 2015)

Cases with GDM at 24-28 weeks (n=24)

- Fasting 54%
- 1-hour 17%
- 2-hour 5%

p<0.01*

*Mc Nemar’s test for correlated proportions

(Daly et al, 2015)
**INCIDENCE OF GDM**

<table>
<thead>
<tr>
<th></th>
<th>Customary</th>
<th>Benchmark</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese women</td>
<td>29%</td>
<td>67%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Selective screening</td>
<td>17%</td>
<td>40%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(Daly et al., 2015 & 2016)

**GDM in obese women (HAPO)**

- Incidence of GDM was 17.9% across 15 centres
- Incidence was 29.1% in obese women post-hoc
- Based on BMI $\times 33.0$ kg/m$^2$ at OGTT
- OGTT at 24-32 weeks
- Overweight women have higher GWG than obese before T3

(Catalano et al., 2012)
GDM and diagnostic criteria post HAPO

- IADPSG/ADA (OR 1.75) 47.0%
- Canadian (OR 2.0) 35.1%
- UK NICE (Cost) 18.8%

(NB) Selective screening (n=202)

(O’Malley et al, 2019)

GDM and maternal obesity (n=116)

- IADPSG/ADA (OR 1.75) 63.5%
- Canadian (OR 2.0) 43.1%
- UK NICE (Cost) 22.4%

(O’Malley et al, 2019)

Learning points

- HAPO diagnostic criteria increase GDM rates
  - especially in obese women
  - especially in USA

- ADA laboratory standards increase GDM rates
  - especially using IADPSG criteria
Learning points

Maternal glucose samples need supervision
- GDM may be missed
- Explains variations in GDM rates?
- Explains poor reproducibility of OGTT?
- Criteria too sensitive?

IV. Maternal obesity and Neural Tube Defects

Maternal obesity and NTDs

- Meta-analysis: 22 studies, > 1.7m women
- Increase OR 1.7 (95% CI 1.5-1.9; p<0.001)
- Linear relationship between increased risk and BMI
- Relationship persisted in studies using aOR

(Huang et al, 2017)
Folate measurements and pregnancy

- Few studies
- Women of childbearing age outside pregnancy
- Lower plasma levels if BMI > 27.0 kg/m² [NHANES 2004]
- Lower folate in white British population with higher BMI
  (Mojtabi 2004; Knight et al, 2015; Maffoni et al, 2017)

Guidelines for obese women

Obese women should take prescription only 5mgs Folic Acid supplementation if, potentially, they may become pregnant in the next 3 months

(National Guidelines UK and Ireland)
Folate and B12 in early pregnancy

- First hospital prenatal visit sociodemographic data
- Convenience recruitment after US
- Computerised by midwives
- Detailed supplement questionnaire
- Supervised 4-day dietary questionnaire
- Weight and height measured cleaned and coded
- Folate, RBC folate, B12 measured

- No difference between obese women and normal women in dietary folate or B12
- No difference between obese women and normal women in Folic Acid supplementation before or during pregnancy

(O’Malley et al, 2019)

Biomarkers and maternal BMI

<table>
<thead>
<tr>
<th></th>
<th>Normal (n=269)</th>
<th>Obese (n=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median serum folate (nmol/l)</td>
<td>36.2</td>
<td>42.0 * (p=0.02)</td>
</tr>
<tr>
<td>Median plasma B12 (pmol/l)</td>
<td>208.0</td>
<td>203.0 * (p=0.03)</td>
</tr>
<tr>
<td>Mean RBC folate (nmol/l)</td>
<td>1139.0</td>
<td>1184.0 NS</td>
</tr>
</tbody>
</table>

(O’Malley et al, 2018)
- CDC predicted 50% fall in NTDs with mandatory folic acid fortification
- Associated with only a 19-26% decrease in NTD rates in USA
- Need mandatory, B12 food fortification?

Learning points

🎓 Obese women should be advised to take higher doses of periconceptual folic acid supplements
🎓 Obese women may need B12 supplements periconceptually

“Great teachers emanate out of passion, knowledge and compassion”

APJ Abdul Kahn
President of India 2002-7
Any questions?

THANK YOU FOR LISTENING