Early life influences on adult chronic disease among aboriginal people

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Increase in type 2 diabetes in children and adolescents in Western Australia

MJA 2004; 180: 459–461 McMahon et al

2: Type 2 diabetes diagnosed each year per 100 000 population <17 years in Western Australia

Overall incidence rate ratio (IRR), 1.27 (95% CI, 1.15–1.41).
IRR for the Indigenous group, 1.23 (95% CI, 1.07–1.40).
IRR for the non-Indigenous group, 1.31 (95% CI, 1.12–1.52).
Cycles of disease risk
Intergenerational effect

Smoking
Malnutrition
Undernutrition
Stress
Hypertension
Diabetes

Experimental animal studies suggest.....
these effects may persist through many generations (i.e. 4-7 generations)!

Source: http://learn.genetics.utah.edu/content/epigenetics/inheritance/
Early life influences on cardio-metabolic disease risk in aboriginal populations

What is the evidence? A systematic review of longitudinal and case-control studies

Review aims

- What is the published evidence for the developmental origins of cardio-metabolic disease in aboriginal populations in Australia, Canada, New Zealand and the United States?
Study inclusion criteria

• Included aboriginal participants

• Used a longitudinal or case control design

• Reported
  - outcomes/exposures during pregnancy or at birth AND
  - disease markers/conditions/mortality for cardio-metabolic diseases in the same individuals at least 3 years later
Flow diagram of the review of citations identified by the search

Citations identified by the search (duplicates removed), n=844

Citations excluded by title and/or abstract review, n=737
Reasons:
- Population (eg. non-aboriginal) n=98 (13%)
- Research type (eg. review) n=76 (10%)
- Study design (eg. data on birth or disease only) n=536 (72%)
- Genetic studies n=27 (4%)

Citations for which full text were obtained, n=107

Citations excluded by review of full text, n=57
Reasons:
- Population (eg. non-aboriginal) n=8
- Research type (eg. review) n=11
- Study design (eg. data on birth or disease only) n=38

Publications included in Review, n=50
Study classification

• Studies with a very low, low or moderate risk of bias were summarised according to the outcome measures
  ▪ metabolic abnormalities
  ▪ adiposity
  ▪ type 2 diabetes
  ▪ kidney disease
  ▪ cardiovascular disease (including hypertension)
### Early Life Exposures and Risk of Type 2 Diabetes/Impaired Glucose Tolerance

| **DIABETES IN UTERO**  
| **(10 Studies)** |
| **↑ RISK OF DIABETES**  
| **(10 STUDIES)** |
| • 9 / 10 studies conducted among Pima Indian population |
| • Siblings born after the mother developed diabetes had a 3.7 times higher risk of developing diabetes compared to siblings born before the diagnosis of diabetes (Dabelea 2000) |

| **BIRTH WEIGHT**  
| **(7 Studies)** |
| **↑ RISK OF DIABETES (6 STUDIES)** |
| • U-shaped relationship among Pima Indian population |
|   - The association between high birth weight and risk of diabetes was related to maternal diabetes during pregnancy |
| • 1 kg increase in birth weight increased the risk of diabetes by 23% among First Nation Canadian people (Dyck 2010) |
| • Low birth weight women have a higher risk of gestational diabetes/diabetes in pregnancy (Williams 1999; Pettit 1998) |

| **BREAST-FEEDING**  
| **(1 Study)** |
| **↓ RISK OF DIABETES**  
| **(1 STUDY)** |
| • Children of non-diabetic mothers who were breastfed had a 44% decreased risk of diabetes compared to children who were not breastfed (Pettit 1998) |

| **RISK OF DIABETES NOT INCREASED**  
| **(1 STUDY)** |
| • Australian study showed that risk of diabetes was not increased among low birth weight individuals compared to normal birth weight (Hoy 1999) |
Systematic Review Diabetes Prevalence Australia Aboriginal

Prevalence

First author surname and year of publication

Any DIP
GDM

10th September 2012
GDM prevalence among Aboriginal and Torres Strait Islander women
GDM Prevalence: 1980-2010, by 5 year age groups
GDM Prevalence: across age groups, by each decade

GDM prevalence among Aboriginal and Torres Strait Islander women

10th September 2012
Percentage of women aged 30 years or older
Total population Western Australian Aboriginal births 1980-2009

>=30

<table>
<thead>
<tr>
<th>Year</th>
<th>Percent</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980-84</td>
<td>13.7%</td>
<td>N=11438</td>
</tr>
<tr>
<td>1985-89</td>
<td>18.4%</td>
<td>N=12871</td>
</tr>
<tr>
<td>1990-94</td>
<td>20.1%</td>
<td>N=14040</td>
</tr>
<tr>
<td>1995-99</td>
<td>21.3%</td>
<td>N=13965</td>
</tr>
<tr>
<td>2000-04</td>
<td>25.8%</td>
<td>N=14012</td>
</tr>
<tr>
<td>2005-09</td>
<td>28.6%</td>
<td>N=15483</td>
</tr>
</tbody>
</table>
Diabetes and hypertension
Total population Western Australian Aboriginal births 1980-2009

[Bar chart showing trends in percentage of births with categories for hypertension, diabetes, and gestational diabetes over different years.]
Implications - What is urgently required?

Intergenerational understanding of type 2 diabetes and diabetes in pregnancy

Systematic approach to diagnosis of diabetes in pregnancy and Optimal treatment of diabetes in pregnancy

Diabetes in pregnancy a MEDICAL EMERGENCY – TIMELY TREATMENT ESSENTIAL

Optimal follow up of women with diabetes in pregnancy at risk for subsequent development of type 2 diabetes
Acknowledgements
Body composition of infants born to mothers with gestational diabetes mellitus

Australasian Diabetes in Pregnancy Society
Annual Scientific Meeting 2012

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Sydney School of Public Health
Royal Prince Alfred Hospital (RPAH) Newborn Care
Royal Prince Alfred Hospital (RPAH) Endocrinology Department
Hypotheses

- There will be a positive relationship between maternal glycemia and neonatal body fat %.

- GDM infants will have higher body fat %, birthweight and larger anthropometrics

- GDM infants with excessive fat will have more adverse neonatal outcomes at birth.
Methodology (1)

- **Population based cross sectional study** at Royal Prince Alfred Hospital (RPAH) Sydney, Sept–Oct 2010

- **Inclusion criteria:**
  - Well term infants (37-42 weeks) within 48 hours of birth

- **Exclusion criteria:**
  - Neonates with congenital anomalies
  - In NICU for >2 days

- Study approved by Ethics Human Research Committee at RPAH and the University of Sydney
Methodology (2)

- **Data from questionnaire and medical record**

- **GDM diagnosis based on the Australian Diabetes in Pregnancy Society (ADIPS) criteria**

- **Glycemic targets achieved by diet, exercise ± insulin**
  - <5.2mmol/L fasting (ADIPS <5.5)
  - <7.5mmol/L 1 hour postprandial (ADIPS <8)

- **Data analysis with SPSS® (v20, IBM®)**
The PEA POD®

- Neonatal body composition (body fat % and fat free mass) measured within 48 hours of birth

- Gold standard = Air Displacement Plethysmography (ADP)
Results (1)

n = 815

Excluded on basis of NICU admission >2 days (n=33; 2 were GDM)

n = 782

Refused participation (n=30)
Early discharge, not approached (n=150)

n = 602

Diabetes
n = 70

Excluded pregestational diabetes (n=3)

NGT
n = 532

GDM
n = 67

11% of our population was GDM
## Results (2)

### Maternal demographic data

<table>
<thead>
<tr>
<th></th>
<th>GDM (n=67)</th>
<th>Non-diabetic (n=532)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>33.2 ± 4.8</td>
<td>32.5 ± 5.1</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight/obese</td>
<td>36%</td>
<td>22%</td>
<td>0.011</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>54%</td>
<td>31%</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Parity &gt;1</strong></td>
<td>54%</td>
<td>43%</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>10%</td>
<td>7%</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>12%</td>
<td>7%</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Diabetes Care  Au C et al 2012 (in press)
Results (3)

GDM control by self-monitoring in 3\textsuperscript{rd} trimester

<table>
<thead>
<tr>
<th>Metric</th>
<th>GDM (n=67)</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mM)</td>
<td>4.8 ± 0.5</td>
<td>5.2</td>
</tr>
<tr>
<td>1 hour postprandial glucose (mM)</td>
<td>6.7 ± 1.1</td>
<td>7.5</td>
</tr>
<tr>
<td>3\textsuperscript{rd} trimester HbA1c</td>
<td>5.4 ± 0.4</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Diabetes Care  Au C et al 2012 (in press)
## Results (6)

### Neonatal body composition

<table>
<thead>
<tr>
<th></th>
<th>GDM (n=67)</th>
<th>Non-diabetic (n=532)</th>
<th>Unadjusted P</th>
<th>Adjusted* P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body fat %</td>
<td>7.9 ± 4.5</td>
<td>9.3 ± 4.3</td>
<td>0.018</td>
<td>0.15</td>
</tr>
<tr>
<td>Fat free mass (g)</td>
<td>2846 ± 338</td>
<td>2959 ± 342</td>
<td>0.010</td>
<td>0.39</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3271 ± 488</td>
<td>3436 ± 471</td>
<td>0.002</td>
<td>0.39</td>
</tr>
</tbody>
</table>

*Adjusted for gestational age, neonatal sex, maternal pregravid BMI, gestational weight gain, parity, maternal ethnicity, maternal smoking status, maternal age, maternal hypertension.
Anthropometric measurements

<table>
<thead>
<tr>
<th></th>
<th>Length</th>
<th>Head circumference</th>
<th>Abdominal circumference</th>
<th>Chest circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unadjusted p</strong></td>
<td>0.002</td>
<td>0.002</td>
<td>0.031</td>
<td>0.014</td>
</tr>
<tr>
<td><strong>Adjusted p</strong></td>
<td>0.49</td>
<td>0.15</td>
<td>0.28</td>
<td>0.15</td>
</tr>
</tbody>
</table>

GDM vs. non-GDM

Results (7)
Summary (1)

- Good glycemic control was achieved in most GDM mothers.

- Newborn %fat was not associated with maternal glycemic control.

- Body composition
  - Birthweight
  - Anthropometrics

No significant difference between GDM and non-diabetic infants
No increase in the following adverse perinatal outcomes in GDM infants:

- Caesarean sections / instrumental vaginal delivery
- Respiratory distress
- NICU admission
- Neonatal hypoglycemia
- Breastfeeding morbidity

But earlier elective delivery
Conclusions

Good glycemic control can prevent the effect of maternal hyperglycemia on accumulation of fetal body fat and poor perinatal outcomes.

Determination of the role of in-utero hyperglycaemia on offspring long term outcomes, coupled with family weight management interventions, will probably be key components to avoiding a future generation of obesity and glucose intolerance.