Mr Tom Charlton

Imperial College London
The impact of HIV infection and ART on the predicted risk of Down’s syndrome

Charlton TG¹, Franklin JM¹, Douglas M¹, Short CE¹, Mills I², Smith R², Clarke A³, Tookey PA⁴, Cortina-Borja M⁴, Smith J¹ and Taylor GP¹

1) Faculty of Medicine, Imperial College London
2) Department of Clinical Chemistry, Birmingham Women's Hospital
3) Department of Sexual Health, St Thomas' Hospital
4) Institute of Child Health, University College London
Down’s syndrome screening is routinely offered to all pregnant women in the UK:

- Combined test (10-14 weeks)
- Triple assay (15-20 weeks)
  - $\beta$- human chorionic gonadotrophin (HCG)
  - $\alpha$– fetoprotein (AFP)
  - Unconjugated oestriol (UE3)
At the time of this work a “high risk” screening result was $>1/250$. 

- Background
- Maternal age
- Maternal weight
- Ethnicity
- Multiple pregnancy
- T1 DM
- HIV?
Does HIV infection lead to more high risk DS screening results?

<table>
<thead>
<tr>
<th>Study</th>
<th>Type (No. Px)</th>
<th>HCG</th>
<th>AFP</th>
<th>UE3</th>
<th>High risk screening vs General population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neale <em>et al.</em> 2001</td>
<td>Retrospective (76)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑ (αFP alone, Triple, Quad)</td>
</tr>
<tr>
<td>Gross <em>et al.</em> 2003</td>
<td>Retrospective (49)</td>
<td>↑</td>
<td>↑</td>
<td>↔</td>
<td>-</td>
</tr>
<tr>
<td>Yudin <em>et al.</em> 2003</td>
<td>Retrospective (34)</td>
<td>↑</td>
<td>↔</td>
<td>↔</td>
<td>↔ (Triple) ↑ (Quad)</td>
</tr>
<tr>
<td>Spencer 2010</td>
<td>Retrospective (52)</td>
<td>↔</td>
<td>↔</td>
<td>↓</td>
<td>-</td>
</tr>
</tbody>
</table>
The story so far

Why is this important?

Diagnostic tests (CVS and amniocentesis):

- 0.5-1% foetal loss (Papantoniou *et al.* 2001)
- HIV transmission (Mandelbrot *et al.* 1996)
- Anxiety
What we did

Are there more “high risk” screening results in the HIV positive population?

- Retrospective, case-control study
- 72 HIV+ve Vs 72 uninfected controls
- Screening, singleton pregnancy’s, 14-18 weeks gestation
- Births took place at St Mary’s Hospital, London between January 2002 and July 2009 (Laboratory BWH)

Do these women have an increased risk of a Down’s syndrome affected pregnancy?

- National Study of HIV in Pregnancy and Childhood (NSHPC) vs National DS register data
**HIV population compared to uninfected controls:**

**HIV+ve (N=72)**
- ✓ ART
- ✓ No ART

“High risk” N=9 (12.5%)

**Uninfected (N=72)**

“High risk” N=0 (0%)

**HIV positive women** were **twice** as likely to receive “high risk” screening results: OR = 2.14, 95% CI = (1.79 - 2.57) p = 0.002
HIV population (without ART) compared to uninfected controls:

- Higher mean hCG MoM (1.64 v 1.07, \( p=0.02 \))
- Higher risk (1/909 v 1/33333, \( p=0.03 \))
- This effect was **not seen** in patients on ART
Key findings 3

Population based data:

- Incidence in HIV positive population, 1/416
- Incidence in general population, 1/633

However, the maternal age differed significantly between the two groups.

Corrected risk = 0

Distributions of maternal age at delivery for the general population and among women enrolled in the NSHPC
Summary

- HIV positive women are twice as likely to receive a “high risk” screening result compared to an uninfected population.

- A particular problem in patients without ART.

- After adjusting for differences in maternal age, population-based evidence does not support a link between HIV serostatus and an increased chance of a DS affected pregnancy.
Main take home messages

1. If patient presents early enough, offer the combined test, 10-14 weeks (Brossard et al. 2008)

2. Preconceptual counselling

3. Know HIV status before interpreting a screening result and referring for invasive diagnostic tests
Acknowledgements

• The Comprehensive Biomedical Research Centre of Imperial College Healthcare NHS Trust.
• The National Study of HIV in Pregnancy and Childhood is currently funded by the Health Protection Agency (grant number GHP/003/013/003).
• MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health.
• Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme.