ATLANTIC DIP: The Impact Of Obesity On Pregnancy Outcome In Glucose Tolerant Women

Lisa A Owens MD¹ Eoin P O’Sullivan MD¹ Breeda Kirwan RN¹
Gloria Avalos MSC¹ Geraldine Gaffney MD RCOG² Fidelma Dunne MD¹PhD
For the ATLANTIC DIP COLLABORATORS

¹Department of Medicine, National University of Ireland, Galway, Ireland
²Department of Obstetrics and Gynaecology, National University of Ireland, Galway, Ireland

Address correspondence to:
Professor Fidelma Dunne
Fidelma.dunne@nuigalway.ie

Submitted 19 May 2009 and accepted 19 November 2009.

This is an uncopyedited electronic version of an article accepted for publication in Diabetes Care. The American Diabetes Association, publisher of Diabetes Care, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of Diabetes Care in print and online at http://care.diabetesjournals.org.
Objective: A prospective study of impact of obesity on pregnancy outcome in glucose tolerant women.

Research Design and Methods: The Irish Atlantic Diabetes in Pregnancy network advocates universal screening for gestational diabetes. Women with normoglycaemia and a recorded booking body mass index (BMI) were included. Maternal and infant outcomes correlated with booking BMI are reported.

Results: 2329 women fulfilled the criteria. Caesarean deliveries increased in OW (OR 1.57, 95% CI 1.24-1.98), OB (OR 2.65, 95% CI 2.03-3.46) women. Hypertensive disorders increased in OW (OR 2.30, 95% CI 1.55-3.40), OB (OR 3.29, 95% CI 2.14-5.05) women. Reported miscarriages increased in OB (OR 1.4, 95% CI 1.11-1.77) women. Mean birth-weight was 3.46kg NBMI, 3.54kg OW, 3.62kg OB (p<0.01) mothers. Macrosomia occurred in 15.5%, 21.4%, 27.8% of babies of NBMI, OW, OB mothers (p<0.01). Shoulder dystocia occurred in 4% (>4Kg) compared to 0.2% (<4kg) babies (p<0.01). Congenital malformation risk increased for OB (OR 2.47, 95% CI, 1.09-5.60) women.

Conclusions: OW and OB glucose tolerant women have greater adverse pregnancy outcomes.
Obesity is now a ‘global pandemic’ (1) and increases the risk of Gestational Diabetes (GDM). Few studies have examined the independent effects of obesity on pregnancy outcome in glucose tolerant women (2-3).

**RESEARCH DESIGN AND METHODS:**

The Atlantic Diabetes in Pregnancy partnership (ATLANTIC DIP) (4) serving a population of 500,000 in 5 centres along the Irish Atlantic seaboard advocates and provides universal screening for GDM using a 75g oral glucose tolerance test (OGTT) at 24-28 weeks. Normoglycaemia is defined as a fasting blood glucose <5.6mmol/L and 2 hour value <7.8mmol/L (5). Maternal Body Mass Index (BMI, kg/m$^2$) was calculated at the first obstetrical visit and defined as normal <25 kg/m$^2$, overweight 25-29.9 kg/m$^2$, OB and obese ≥30 kg/m$^2$. Maternal outcomes included Caesarean deliveries, antepartum and postpartum haemorrhage (APH, PPH), pregnancy induced hypertension (PIH) and Pre-eclampsia (PET). Fetal/infant outcomes included gestational weight at delivery, macrosomia, shoulder dystocia, major congenital malformations, miscarriage, stillbirth, neonatal death and perinatal mortality. Statistical analyses were carried out using the Statistical Package for the Social Sciences, SPSS version 15.0. Significance was achieved at p<0.05.

**RESULTS**

**Maternal Outcomes:** Two thousand three hundred and twenty nine women, mean age (sd) 31.4 (+/-5.4) years, 90% Caucasian with a recorded booking BMI and a normal OGTT were included. Caesarean deliveries increased from 16.4% to 23.4% to 32.6% in NBMI, OW, OB women (p<0.01). The trend was similar for elective CS (ELCS) increasing from 6.5% to 11% to 16.5% in NBMI, OW, OB women (p<0.01). There was no correlation between increasing maternal age and increasing BMI. PIH increased from 4.3% to 9% to 11.3% in NBMI, OW, OB women (p<0.01). PET risk doubled from 2.7% to 4.7% to 6% in NBMI, OW, OB women (p<0.01). The overall risk of hypertensive disorders increased from 5% to 9.7% to 12.7% in NBMI, OW, OB women (p<0.01). The OR of having a pregnancy complicated by hypertension was 2.30 ([95% CI 1.55-3.40] p<0.01) OW and 3.29 ([95% CI 2.14-5.05] p<0.01) OB women (Table 1). There was no significant difference in the rates of APH or PPH between groups.

**Fetal/Infant Outcomes:** 41.2% of OB women had a history of >1 miscarriage, compared to 34.7%, 32.5% OW and NBMI women (p<0.01). The OR of a history of miscarriage was 1.4 (95% CI 1.11-1.77) OB (p<0.01). There was a linear increase in birth weight across each BMI group. Mean (+sd) birth weight was 3.46(+/-0.53), 3.54(+/-0.59), 3.62 (+/-0.55) kg in babies of NBMI, OW, OB women (p<0.01). The percentage of macrosomic babies (> 4kg) increased from 15.5% to 21.4% to 27.8% in NBMI, OW, OB women (p<0.01). 4.1% of babies (>4kg) compared to 0.2% of babies (< 4kg) had shoulder dystocia (p<0.01). 37 babies (1.6%) had congenital malformations. The OR of a malformation was 2.47 [95% CI 1.09-5.60] p=0.03) OB women. 14 (0.6%) stillbirths, 2 (0.1%) neonatal deaths occurred with a PMR of 6/1000. BMI was not a positive predictor for these outcomes.

**CONCLUSIONS**

Obesity is a risk factor for adverse pregnancy outcome but the potential contribution from undiagnosed hyperglycaemia is not always excluded (6-8). We excluded diabetes and demonstrated increased adverse events with
increased BMI. Rates of EMCS/ELCS increased in OW /OB women. The higher rates of EMCS are likely to be more than a reflection of local obstetric practice as 14.2% infants delivered by EMCS versus 6% by ELCS and 3.6% vaginally were admitted to NICU (p<0.01). Prevalence of PIH/PET was increased in OW and OB women. An overview of 13 studies involving a million women suggests the risk of PET doubles with every 5-7kg/m² increase in BMI (9). Our findings were broadly similar with an approximate doubling of risk of PIH in the presence of obesity. This is a significant finding given that hypertensive disorders are the third-leading cause of maternal death (10) with a suggestion that long-term cardiovascular mortality may be increased (6).

Macrosomia is more common in OB women (11). In addition to birth injury macrosomia is linked to increased obesity and dysglycemia in adolescence (12). We found a strong association between obesity, macrosomia and shoulder dystocia. A meta-analysis by Stothard (13) showed that obese women are at increased risk of congenital malformations. The authors recognised in their conclusion that some of these adverse outcomes may be due to undiagnosed hyperglycaemia. We found a significantly higher rate of congenital malformations in OB women (OR 2.47) but had excluded diabetes.

Previous studies have tried to disentangle the effects of obesity and diabetes on pregnancy outcome. Jensen found an increased risk of adverse events in OW/OB glucose tolerant Danish women (2). These women were selected on the basis of increased risk of GDM thereby limiting the application of the findings to the general population. Our study was in an unselected population offered universal screening for GDM and the results are therefore more applicable to the general obstetric population. In an earlier study Jensen demonstrated increasing risk of shoulder dystocia and macrosomia with increasing increments in fasting and 2 hour glucose values but patients with impaired glucose tolerance were not excluded (3). We recognise that despite excluding women with GDM/IGT there is evidence that even lesser degrees of hyperglycemia may still carry additional risk of adverse outcomes, as demonstrated in the HAPO study (14).

Obesity confers an increased life-time risk for type 2 diabetes and research has offered potential interventions to retard this (15). Identifying obese women and providing interventions is essential for long-term diabetes prevention. Obese women could be offered pre-pregnancy care (PPC) with a focus on promoting normal BMI prior to their next pregnancy. This would potentially reduce adverse maternal outcomes. Reducing BMI would also impact on the offspring in the antenatal and postnatal periods. Further studies are needed to compare outcomes of obese women who undergo intensive PPC compared to those with no intervention.

ACKNOWLEDGEMENTS
Parts of this article were presented as oral communications at the American Diabetes Association (ADA June 2009) and Diabetes Pregnancy Subgroup (DP SG) of the European Association Study Diabetes (EASD September 2009).

We are grateful to the staff and patients along the Atlantic seaboard, to collaborators at each centre and to the Health Research Board for funding.
REFERENCES

15. Robert E. Ratner, Costas A. Christophi, Boyd E. Metzger, Dana Dabelea, Peter H. Bennett, Xavier Pi-Sunyer, Sarah Fowler, Steven E. Kahn, Prevention of Diabetes in Women

Table 1. Logistic regression predicting Caesarean Section and Hypertension Disorders of Pregnancy)in women under study.

<table>
<thead>
<tr>
<th></th>
<th>Caesarean Section</th>
<th>Hypertensive Disorder of Pregnancy*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>CI</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.57</td>
<td>1.24-1.98</td>
</tr>
<tr>
<td>Obese</td>
<td>2.65</td>
<td>2.03-3.46</td>
</tr>
<tr>
<td>White</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Black African</td>
<td>1.14</td>
<td>0.52-2.50</td>
</tr>
<tr>
<td>Asian</td>
<td>1.03</td>
<td>0.52-2.03</td>
</tr>
<tr>
<td>Other</td>
<td>2.50</td>
<td>1.01-6.15</td>
</tr>
<tr>
<td>Age</td>
<td>1.06</td>
<td>1.036-1.08</td>
</tr>
<tr>
<td>Parity 0</td>
<td>1.00</td>
<td>0.0001</td>
</tr>
<tr>
<td>Parity 1-3</td>
<td>0.66</td>
<td>0.53-0.81</td>
</tr>
<tr>
<td>Parity ≥4</td>
<td>0.15</td>
<td>0.06-0.40</td>
</tr>
</tbody>
</table>