

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, MD, PHD¹
FOR THE ATLANTIC DIP
COLLABORATORS

OBJECTIVE — A prospective study of the 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 normoglycemia and a recorded booking BMI were included. Maternal and infant outcomes correlated with booking BMI are reported.

RESULTS — A total of 2,329 women fulfilled the criteria. Caesarean deliveries increased in overweight (OW) (odds ratio 1.57 [95% CI 1.24–1.98]) and obese (OB) (2.65 [2.03–3.46]) women. Hypertensive disorders increased in OW (2.30 [1.55–3.40]) and OB (3.29 [2.14–5.05]) women. Reported miscarriages increased in OB (1.4 [1.11–1.77]) women. Mean birth weight was 3.46 kg in normal BMI (NBMI), 3.54 kg in OW, and 3.62 kg in OB ($P < 0.01$) mothers. Macrosomia occurred in 15.5, 21.4, and 27.8% of babies of NBMI, OW, and OB mothers, respectively ($P < 0.01$). Shoulder dystocia occur in 4% (>4 kg) compared with 0.2% (<4 kg) babies ($P < 0.01$). Congenital malformation risk increased for OB (2.47 [1.09–5.60]) women.

CONCLUSIONS — OW and OB glucose-tolerant women have greater adverse pregnancy outcomes.

Diabetes Care 33:577–579, 2010

Obesity is now a global pandemic (1) and increases the risk of gestational diabetes mellitus (GDM). Few studies (2,3) have examined the independent effects of obesity on pregnancy outcome in glucose-tolerant women.

RESEARCH DESIGN AND METHODS

The Atlantic Diabetes in Pregnancy Partnership (ATLANTIC DIP) (4), serving a population of 500,000 in five centers along the Irish Atlantic seaboard, advocates and provides universal screening for GDM using a 75-g oral glucose tolerance test (OGTT) at 24–28 weeks. Normoglycemia is defined as a fasting blood glucose <5.6 mmol/l and 2-h value <7.8 mmol/l (5). Maternal BMI

(kg/m²) was calculated at the first obstetrical visit and defined as <25 kg/m² normal BMI (NBMI), overweight (OW) 25–29.9 kg/m², and obese (OB) ≥ 30 kg/m². Maternal outcomes included caesarean deliveries, antepartum (APH) and postpartum (PPH) hemorrhage, pregnancy-induced hypertension (PIH), and preeclampsia (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 version 15.0. Significance was achieved at $P < 0.05$.

RESULTS

Maternal outcomes

A total of 2,329 women, mean \pm SD age 31.4 \pm 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, and OB women, respectively ($P < 0.01$). The odds ratio (OR) of a caesarean delivery was 1.57 (95% CI 1.24–1.98, $P < 0.01$) for OW and 2.65 (2.03–3.46, $P < 0.01$) for OB women (Table 1). The risk of an emergency caesarean delivery increased from 10 to 12.4 to 16.1% in NBMI, OW, and OB women, respectively ($P < 0.01$). The trend was similar for elective caesarean delivery, increasing from 6.5 to 11 to 16.5% NBMI, OW, and OB women, respectively ($P < 0.01$). There was no correlation between increasing maternal age and increasing BMI.

PIH increased from 4.3 to 9 to 11.3% in NBMI, OW, and OB women, respectively ($P < 0.01$). PET risk doubled from 2.7 to 4.7 to 6% in NBMI, OW, and OB women, respectively ($P < 0.01$). The overall risk of hypertensive disorders increased from 5 to 9.7 to 12.7% in NBMI, OW, and OB women, respectively ($P < 0.01$). The OR of having a pregnancy complicated by hypertension was 2.30 (95% CI 1.55–3.40, $P < 0.01$) in OW and 3.29 (2.14–5.05, $P < 0.01$) in OB women (Table 1). There was no significant difference in the rates of APH or PPH between groups.

Fetal/infant outcomes

A total of 41.2% of OB women had a history of more than one miscarriage, compared with 34.7 and 32.5% in OW and NBMI women, respectively ($P < 0.01$). The OR of a history of miscarriage was 1.4 (95% CI 1.11–1.77 in OB women, $P < 0.01$). There was a linear increase in birth weight across each BMI group. Mean (\pm SD) birth weight was 3.46 \pm 0.53, 3.54 \pm 0.59, and 3.62 \pm 0.55 kg in babies of NBMI, OW, and OB women, respectively ($P < 0.01$). The percentage of macrosomic babies (>4 kg) increased from 15.5 to 21.4 to 27.8% in NBMI, OW, and OB

From the ¹Department of Medicine, National University of Ireland, Galway, Ireland; and the ²Department of Obstetrics and Gynecology, National University of Ireland, Galway, Ireland.

Corresponding author: Fidelma Dunne, fidelma.dunne@nuigalway.ie.

Received 19 May 2009 and accepted 19 November 2009. Published ahead of print at <http://care.diabetesjournals.org> on 19 January 2010. DOI: 10.2337/dc09-0911.

© 2010 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Table 1—ORs and CIs of caesarean section and hypertensive disorders of pregnancy

	Caesarean section		Hypertensive disorder of pregnancy*	
	OR (95% CI)	P	OR (95% CI)	P
Normal weight	1.00		1.00	
Overweight	1.57 (1.24–1.98)	0.0001	2.30 (1.55–3.4)	0.0001
Obese	2.65 (2.03–3.46)	0.0001	3.29 (2.14–5.05)	0.0001
White	1.00		1.00	
Black African	1.14 (0.52–2.50)	0.744	1.90 (0.70–1.56)	0.206
Asian	1.03 (0.52–2.03)	0.927	0.81 (0.25–2.66)	0.723
Other	2.50 (1.01–6.15)	0.047	1.58 (0.34–7.43)	0.560
Age	1.06 (1.036–1.08)	0.0001	1.00 (0.97–1.04)	0.870
Parity				
0	1.00	0.0001	1.00	
1–3	0.66 (0.53–0.81)	0.0001	1.77 (0.65–4.82)	0.261
≥4	0.15 (0.06–0.40)	0.0001	0.73 (0.27–1.95)	0.527

*Pregnancy-induced hypertension or preeclampsia.

women, respectively ($P < 0.01$). A total of 4.1% of babies (>4 kg) compared with 0.2% of babies (<4 kg) had shoulder dystocia ($P < 0.01$). Thirty-seven babies (1.6%) had congenital malformations. The OR of a malformation was 2.47 (1.09–5.60, $P = 0.03$) in OB women. Fourteen (0.6%) stillbirths and two (0.1%) neonatal deaths occurred with a PMR of 6 of 1,000. 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 hyperglycemia is not always excluded (6–8). We excluded diabetes and demonstrated increased adverse events with increased BMI. Rates of emergency caesarean delivery/elective caesarean delivery increased in OW and OB women. The higher rates of emergency caesarean delivery are likely to be more than a reflection of local obstetric practice, as 14.2% infants delivered by emergency caesarean delivery versus 6% by elective caesarean delivery and 3.6% vaginally were admitted to the neonatal intensive care unit ($P < 0.01$). Prevalence of PIH/PET was increased in OW and OB women. An overview of 13 studies involving a million women suggests that the risk of PET doubles with every 5–7 kg/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 et al. (13) showed that obese women are at increased risk of congenital malformations. The authors recognized in their conclusion that some of these adverse outcomes may be due to undiagnosed hyperglycemia. 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 et al. (2) found an increased risk of adverse events in OW/OB glucose-tolerant Danish women. 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-h glucose values, but patients with impaired glucose tolerance were not excluded (3). We recognize that despite excluding women with GDM/impaired glucose tolerance, there is evidence that even lesser degrees of hyperglycemia may still carry additional risk of adverse outcomes, as demonstrated in

the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (14).

Obesity confers an increased lifetime 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 prepregnancy care with a focus on promoting NBMI prior to their next pregnancy. This would potentially reduce adverse maternal outcomes. Reducing BMI would also affect the offspring in the antenatal and postnatal periods. Further studies are needed to compare outcomes of obese women who undergo intensive prepregnancy care compared with those with no intervention.

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

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

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

References

1. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation*. Geneva, World Health Org., 2000 (Tech. Rep. Ser., no. 2000)
2. Jensen DM, Damm P, Sorensen B, Mølsted-Pedersen L, Westergaard JG, Ovesen P, Beck-Nielsen H. Pregnancy outcome and prepregnancy body mass index in 2459 glucose-tolerant Danish women. *Am J Obstet Gynecol* 2003;189:239–244
3. Jensen DM, Ovesen P, Beck-Nielsen H, Mølsted-Pedersen L, Sørensen B, Vinter C, Damm P. Gestational weight gain and pregnancy outcomes in 481 obese glucose-tolerant women. *Diabetes Care* 2005;28:2118–2122
4. Dunne FP, Avalos G, Durkan M, Mitchell Y, Gallacher T, Keenan M, Hogan M, Carmody LA, Gaffney G, the ATLANTIC DIP Collaborators. Pregnancy outcome for women with pregestational diabetes along the Irish Atlantic seaboard. *Diabetes Care* 2009;32:1205–1206
5. American Diabetes Association. Diagnosis and classification of diabetes. *Diabetes Care* 2008;31(Suppl. 1):S55–S60
6. Samuels-Kalow ME, Funai EF, Buhimschi C, Norwitz E, Perrin M, Calderon-Margalit R, Deutsch L, Paltiel O, Friedlander Y, Manor O, Harlap S. Prepregnancy body

- mass index, hypertensive disorders of pregnancy, and long-term maternal mortality. *Am J Obstet Gynecol* 2007;197:490.e1–490.e6
7. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Regan L, Robinson S. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *Int J Obes* 2001;25:1175–1182
 8. Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, Saade G, Eddleman K, Carter SM, Craigo SD, Carr SR, D'Alton, the ME FASTER Research Consortium. Obesity, obstetric complications and Cesarean delivery rate: a population-based screening study. *Am J Obstet Gynecol* 2004;190:1091
 9. O'Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of pre-eclampsia: a systematic overview. *Epidemiology* 2003;14:368–374
 10. World Health Organization. The World Health Report 2005: Make Every Mother and Child Count [article online], 2005. World Health Org., Geneva. Available at www.who.int/whr/2005/en. Accessed 20 November 2008
 11. Williams RL, Creasy RK, Cunningham GC, Hawes WE, Norris FD, Tashiro M. Fetal growth and perinatal viability in California. *Am J Obstet Gynecol* 1982;59:624
 12. Sorensen HT, Sabroe S, Rothman KJ, Gillman M, Fischer P, Sorensen TI. Relation between weight and length at birth and body mass index in young adulthood: cohort study. *BMJ* 1997;315:1137
 13. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *J Am Med Assoc* 2009;301:636–650
 14. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS, Sacks DA. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991–2002
 15. Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, Fowler S, Kahn SE, the Diabetes Prevention Program Research Group. Effects of metformin and lifestyle interventions. *J Clin Endocrinol Metab* 2008;93:4774–4779