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Obstetric and perinatal outcomes in pregnancies complicated by Type 1 and Type 2 diabetes: influences of glycaemic control, obesity and social disadvantage

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Abstract

Aims—To compare obstetric and perinatal outcomes in women with Type 1 and Type 2 diabetes and relate these to maternal risk factors.

Methods—Prospective cohort study of 682 consecutive diabetic pregnancies in East Anglia during 2006–2009. Relationships between congenital malformation, perinatal mortality and perinatal morbidity (large for gestational age, preterm delivery, neonatal care) with maternal age, parity, ethnicity, glycaemic control, obesity and social disadvantage were examined using bivariable and multivariate models.

Results—There were 408 (59.8%) Type 1 and 274 (40.2%) Type 2 diabetes pregnancies. Women with Type 2 diabetes were older ($P < 0.001$), heavier ($P < 0.0001$), more frequently multiparous ($P < 0.001$), more ethnically diverse ($p < 0.0001$) and more socially disadvantaged ($P = 0.0004$). Although women with Type 2 diabetes had shorter duration of diabetes ($P < 0.0001$) and better pre-conception glycaemic control [HbA_{1c} 52 mmol/mol (6.9%) Type 2 diabetes vs. 63 mmol/mol (7.9%) Type 1 diabetes; $p < 0.0001$], rates of congenital malformation and perinatal mortality were comparable. Women with Type 2 diabetes had fewer large-for-gestational-age infants (37.6 vs. 52.9%, $P < 0.0008$), fewer preterm deliveries (17.5 vs. 37.1%, $P < 0.0001$) and their offspring had fewer neonatal care admissions (29.8 vs. 43.2%, $P = 0.001$). Third trimester HbA_{1c} (OR 1.35, 95% CI 1.09–1.67, $P = 0.006$) and social disadvantage (OR 0.80, 95% CI 0.67–0.98; $P = 0.03$) were risk factors for large for gestational age.

Conclusions—Despite increased age, parity, obesity and social disadvantage, women with Type 2 diabetes had better glycaemic control, fewer large-for-gestational-age infants, fewer preterm

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Competing interests

Nothing to declare.

deliveries and fewer neonatal care admissions. Better tools are needed to improve glycaemic control and reduce the rates of large for gestational age, particularly in Type 1 diabetes.

Keywords

large for gestational age; macrosomia; pregnancy; Type 1 diabetes; Type 2 diabetes

Introduction

The Confidential Enquiry for Maternal and Child Health reported comparable obstetric and perinatal outcomes of women with Type 1 and Type 2 diabetes [1]. More recently, a systematic review of 33 studies suggested that offspring of mothers with Type 2 diabetes have increased perinatal mortality, without increased congenital malformation [2]. However, many studies were retrospective, included relatively small numbers of pregnancies with Type 2 diabetes and/or had incomplete data on confounding maternal risk factors. Thus, the relative contributions of maternal demographics (age, parity, ethnicity, social disadvantage) and potentially modifiable risk factors (glycaemic control, obesity, teratogenic medications) to adverse perinatal outcome in Type 2 diabetes remain unclear.

Previous studies suggest comparable maternal glycaemic control and perinatal morbidity, including rates of large for gestational age, preterm delivery and neonatal care in Type 1 and Type 2 diabetes [1,3]. In Type 1 diabetes, rates of large for gestational age are increasing, perhaps attributable to increased maternal obesity and reduced microvascular complications [4]. By contrast, there is clear evidence that intensive management, with diet, insulin and/or metformin, is associated with reduced large for gestational age, preterm delivery and neonatal care in gestational diabetes [5]. Maternal glycaemic control is the strongest predictor of perinatal morbidity in gestational diabetes [6]. As new evidence emerges that pregnant women with Type 2 diabetes may have a milder glycaemic disturbance and better glycaemic control than women with Type 1 diabetes [2], this would indicate a potential for better perinatal outcomes in women with well-controlled Type 2 diabetes.

We previously documented the opportunities for improvement in the management of women with pregestational diabetes [3]. We then implemented a regional campaign to provide better organized care, particularly for centres where poor pregnancy preparation and delayed antenatal presentation were prevalent. Details of the pre-conception counselling and pre-pregnancy care programme are reported elsewhere [7,8]. The aim of this study was to compare obstetric and perinatal outcomes in women with Type 1 and Type 2 diabetes. We also aimed to relate these outcomes to maternal risk factors; namely, age, parity, obesity, ethnicity, social disadvantage, glycaemic control and type of diabetes.

Patients and methods

The East Anglia Study Group for Improving Pregnancy Outcomes in women with Diabetes (EASIPOD) was established with interdisciplinary representation from 10 participating regional maternity units. We included all pregnancies in women with pregestational Type 1 or Type 2 diabetes who delivered between 1 October 2006 and 30 September 2009.

The study was approved by the research ethics committees of Suffolk, Norfolk and Cambridgeshire (06/Q0102/116).

Data collection

Pregnancies were registered as soon as contact with the diabetes antenatal team was established. A standardized data collection proforma was completed within 3 months of the

end of each pregnancy. A central study coordinator facilitated data validation, timely data collection and entry onto the central database. To comply with NHS Trust information governance and data protection procedures, the central data set was anonymized. It is therefore possible that some women were included for more than one pregnancy.

Maternal data

Pregestational diabetes was defined as Type 1 or Type 2 diabetes diagnosed at least 12 months before pregnancy. Quintiles of deprivation were derived from the postcode of residence using Index of Multiple Deprivations (IMD) scores specific to the East of England [9]. Ethnicity was classified as White (British, Irish, and any other White background), Asian (Bangladeshi, Far East Asian, Indian, Middle Eastern, Pakistani, South-East Asian) and other. Microvascular complications were determined by local diabetologists using national diabetes audit definitions for retinopathy, neuropathy and nephropathy. Maternal HbA_{1c} levels were recorded up to 6 months pre-conception and at 4- to 8-weekly intervals throughout pregnancy. Samples were assayed using Diabetes Control and Complications Trial (DCCT)-aligned methodology (normal reference range 3.6–5.8%) in accredited laboratories with all centres participating in the national external quality assurance programme.

Pregnancies were described as ‘planned’ if contraception was discontinued for the purposes of pregnancy. All other pregnancies were unplanned. Pre-conception counselling was documented evidence of a discussion regarding the pregnancy risks associated with diabetes. Pre-pregnancy care was defined as a woman working in partnership with health professionals to optimize pregnancy outcome [7].

Obstetric outcome measures

Miscarriage was defined as the spontaneous ending of pregnancy before 24 weeks. Congenital malformations were classified according to the European Surveillance of Congenital Anomalies (EUROCAT) system. Stillbirth was fetal death after 24 weeks and neonatal death as death of a live-born infant before 28 days. Serious adverse pregnancy outcome was a major congenital malformation (including termination for malformation), stillbirth or neonatal death. Because of the increased risks associated with twin pregnancy, all obstetric and perinatal morbidity analyses were performed in singleton pregnancies.

Perinatal morbidity measures

Preterm delivery was defined as before 37 weeks and early preterm delivery as before 34 weeks. Infant birthweight, gender and gestational age were used to calculate customized birthweight percentiles adjusted for maternal ethnicity, height, weight and parity [10]. Large for gestational age was defined as birthweight ≥ 90th centile, extreme large for gestational age as birthweight ≥ 97.7th centile and small for gestational age as birthweight < 10th centile.

Statistical analyses

Univariate analyses were performed using χ^2 -tests for categorical variables and *t*-tests for continuous variables. For multivariate analyses, logistic regression was used. To handle missing data (typically < 20 cases per variable), five multiply imputed data sets were generated using the ‘mi’ package in R. In this package, a chained equation approach is used to impute the missing data, based on linear combinations of the predictor variables. Semi-continuous variables were handled using the appropriate transformation to a fully continuous variable [11]. Diagnostic plots showed the imputation models fitted the data well. Separate

logistic regression models for each imputed data set were combined using the Rubin formulae to generate the final estimates presented in the paper [11].

The number of births for the 10 centres in this region is approximately 50 000 live births, of which 200 are complicated by pregestational diabetes. We calculated that a sample size of 528 infants would give 80% power to detect a 25% relative reduction in the rate of large for gestational age.

The hypotheses of interest in this study were whether serious adverse outcome (major malformation and perinatal mortality) and perinatal morbidity (large for gestational age, preterm delivery and neonatal care) were different, independent of potential confounding variables, in the offspring of mothers with Type 2 compared with Type 1 diabetes. The model therefore included maternal age, parity, ethnicity, BMI, Index of Multiple Deprivations quintile (as a marker of social disadvantage), diabetes type and duration, HbA_{1c}, pre-pregnancy care, presence of microvascular complications and smoking history.

Results

During the 3-year study period, 686 pregnancies were registered. Four pregnancies attributed to other types of diabetes were excluded. For the remaining 682 pregnancies, 408 (59.8%) were complicated by Type 1 diabetes and 274 (40.2%) by Type 2 diabetes. Their maternal characteristics, diabetes status and pregnancy preparation are shown in Table 1. Details of the obstetric and perinatal outcomes for 667 singleton pregnancies (excluding 11 twin pregnancies and four pregnancies in women with Type 1 diabetes who transferred out of region for delivery) are shown in Table 2.

Maternal characteristics by type of diabetes

Women with Type 2 diabetes were, as expected, older ($P < 0.0001$), heavier ($P < 0.0001$), more frequently multiparous ($P < 0.0001$), more likely to live in a deprived area ($P = 0.0004$) and to belong to an ethnic minority group ($P < 0.0001$) than women with Type 1 diabetes (Table 1). They had shorter duration of diabetes ($P < 0.0001$) and were less likely to have microvascular complications ($P < 0.0001$). There were no differences between their pregnancy intentions (approximately 50% planned), but women with Type 2 diabetes were less likely to have pre-conception counselling ($P < 0.0001$), pre-conception folic acid ($P = 0.009$) and pre-pregnancy care ($P = 0.0009$).

Women with Type 2 diabetes were more likely to use potentially harmful medications at conception; statins (11.7 vs. 1.7%; $P < 0.0001$), ACE inhibitors (7.3 vs. 1.5%; $P = 0.0002$) and glitazones (8.0 vs. 0.0%; $P < 0.0001$). Some women with Type 1 diabetes (3.2%) and over half the women with Type 2 diabetes (55.5%) used metformin at conception. Despite suboptimal pregnancy preparation, women with Type 2 diabetes had significantly better glycaemic control than women with Type 1 diabetes, with HbA_{1c} levels that were on average 1% lower before pregnancy and remained at least 0.5% lower throughout pregnancy ($P = 0.0001$).

Obstetric and perinatal outcomes

There were 124 (18.5%) early pregnancy losses, 99 (14.7%) spontaneous miscarriages, 25 (3.7%) terminations of which nine (1.3%) were performed as a result of congenital malformation (Table 2). From the 543 pregnancies 24 weeks' gestation, there were an additional 14 malformations, giving a total of 23 major congenital malformations (congenital malformation rate 41.6/1000 births). There were 543 births, including seven stillbirths and 536 live births (stillbirth rate 12.9/1000 births). Three neonatal deaths occurred, all in women with Type 1 diabetes (neonatal death rate 5.6/1000 live births),

giving a total of 10 perinatal deaths (perinatal mortality rate 18.4/1000 births). The 23 congenital malformations, seven stillbirths and three neonatal deaths resulted in a total of 33 (6.0%) serious adverse outcomes. Rates of congenital malformation and perinatal mortality were comparable between Type 1 and Type 2 diabetes (67/1000 vs. 50/1000; $P = 0.5$).

Risk factors for congenital malformation and perinatal mortality

Among the entire cohort, HbA_{1c} at booking (OR 1.46, 95% CI 1.16–1.85; $P = 0.001$ per 1% HbA_{1c} increase) and lack of pre-pregnancy care (OR 0.2, 95% CI 0.05–0.89; $P = 0.03$) were the only significant risk factors for congenital malformation and perinatal mortality. Duration of diabetes and Type 1 diabetes approached but did not quite reach significance ($P = 0.06$ and 0.07). In Type 2 diabetes, HbA_{1c} at booking was the only significant risk factor (OR 1.45, 95% CI 0.99–2.12; $P = 0.05$ per 1% increase in HbA_{1c}), with no other variables, including maternal age, parity, obesity, ethnicity, pre-pregnancy care, social disadvantage or metformin, reaching significance.

Obstetric and perinatal morbidity

Comparing their delivery patterns, women with Type 1 diabetes were significantly more likely to be delivered by Caesarean section (63.5% Type 1 vs. 51.4% Type 2 diabetes; $P = 0.006$). Thus, almost half the mothers with Type 2 diabetes had a vaginal delivery (48.6% Type 2 vs. 36.5% Type 1 diabetes; $P = 0.003$). The offspring of women with Type 2 diabetes were also less likely to be delivered preterm (17.5% Type 2 vs. 37.1% Type 1 diabetes; $P < 0.0001$) or to be admitted for more than the standard level of neonatal care (29.8% Type 2 vs. 43.2% Type 1 diabetes; $P = 0.001$). There were significantly fewer large for gestational age offspring (37.6% Type 2 vs. 52.9% Type 1 diabetes; $P = 0.0008$) and extreme large for gestational age offspring (25.7% Type 2 vs. 35.7% Type 1 diabetes; $P = 0.02$) of mothers with Type 2 diabetes. Rates of small for gestational age in mothers with Type 2 diabetes (11.4%) approached the expected 10%, with a notable lack of small for gestational age offspring (4.9%) in mothers with Type 1 diabetes ($P = 0.009$).

Risk factors for large for gestational age

To determine the extent to which maternal risk factors (age, parity, obesity, ethnicity, glycaemic control, etc.) accounted for the different rates of large for gestational age in mothers with Type 1 and Type 2 diabetes, logistic regression analyses were performed. Among the entire cohort ($n = 667$), the risk factors for delivering a large-for-gestational-age infant were third trimester HbA_{1c} (OR 1.35, 95% CI 1.09–1.67; $P = 0.006$) and social disadvantage (OR 0.80, 95% CI 0.66–0.98; $P = 0.03$). No other factors, including age, parity, ethnicity, obesity, microvascular complications and cigarette smoking, were significant, although duration of diabetes (OR 1.04, 95% CI 1.00–1.09; $p = 0.06$) and HbA_{1c} at booking (OR 1.2, 95% CI 0.99–1.47; $P = 0.06$) both approached significance. In Type 2 diabetes ($n = 270$), social disadvantage remained significant (OR 0.71, 95% CI 0.53–0.95; $P = 0.02$) along with maternal obesity (OR 1.07, 95% CI 1.00–1.14; $P = 0.04$). There was no difference in the HbA_{1c} levels, obstetric outcomes or perinatal morbidity of women with and without metformin (data not shown).

Discussion

The obstetric risk factors of pregnant women with Type 2 diabetes in this cohort were striking. Compared with women with Type 1 diabetes, they were older (by approximately 4 years), 60% lived in socially disadvantaged areas, 70% were multiparous and 90% were overweight or obese. While ethnic diversity, religious and cultural beliefs may influence attitudes to contraception and family planning, women with Type 2 diabetes were poorly prepared for pregnancy, with suboptimal folic acid and pre-pregnancy care. Approximately

20% of women with Type 2 diabetes (compared with < 3% with Type 1 diabetes) used potentially harmful medications at conception. Despite these additional risk factors, the offspring of women with Type 2 diabetes had no increased risk of congenital malformation or perinatal mortality. Furthermore, infants of mothers with Type 2 diabetes had significantly less perinatal morbidity; they were less likely to be born large for gestational age, delivered preterm or admitted for neonatal care.

We found that HbA_{1c} at booking was the only independent risk factor for congenital malformation and perinatal mortality in Type 2 diabetes. Our findings are in contrast to studies in the background maternity population [12] and in gestational diabetes [13,14]. The Irish Atlantic Diabetes In Pregnancy (ATLANTIC DIP) study found that obesity increased the risk of miscarriage, congenital malformation and other maternal (Caesarean section) and perinatal complications (large for gestational age) in glucose-tolerant women [12]. Others report the contributions of maternal age [15], oral hypoglycaemic agents [3,16], ACE inhibitors [17] and statins [18] to risk of congenital malformation. Two studies from Spain [13,14] observed an additional risk of malformation when gestational diabetes and obesity co-exist, suggesting different contributions of obesity and hyperglycaemia.

Confirming the contribution of glycaemic control in women with Type 2 diabetes is important, as, unlike demographic factors and, to a lesser extent, obesity, glycaemic control is potentially modifiable. The tighter glycaemic control achieved by women with Type 2 diabetes is in contrast to the previous East Anglia audit and nationwide Confidential Enquiry [1,3]. We speculate that the recent improvements represent better community management of Type 2 diabetes and/or a milder glycaemic disturbance and less glycaemic variability [2,19,20]. We previously described the rapid early improvement in glycaemic control in Type 2 diabetes and the stagnation or late increase in HbA_{1c} in Type 1 diabetes [19,21]. This study suggests that HbA_{1c} may also increase in late gestation in Type 2 diabetes, perhaps because of increasing insulin resistance and/or the failure of HbA_{1c} measurement to adequately reflect glycaemic control in late pregnancy [22]. We confirm the association between third trimester glycaemic control and perinatal morbidity, suggesting that interventions to improve late gestation glycaemic control may reduce rates of large for gestational age, preterm delivery and neonatal care admission.

During the East Anglia audit of 1999–2004 [3], rates of large for gestational age were comparable in Type 1 and Type 2 diabetes (46.5 vs. 46.9%), findings similar to the UK Confidential Enquiry [23] and a systematic review [2]. Balsells *et al.* found a reduction in diabetic ketoacidosis, Caesarean section delivery and a trend towards reduced neonatal hypoglycaemia in Type 2 diabetes [2]. In contrast to our findings, they did not find any differences in large for gestational age, preterm delivery or neonatal care. Our current audit, performed in the same regional maternity units as during 1999–2004, found a significant difference in large-for-gestational-age rates between Type 1 (52.9%) and Type 2 diabetes (37.6%). This demonstrates improvements in Type 2 diabetes, but confirms the increasing prevalence of large for gestational age in Type 1 diabetes, described in a recent longitudinal Swedish study [4]. This suggests that more intensive input is required to improve third trimester glycaemic control and perinatal outcomes in Type 1 diabetes. Our continuous glucose monitoring randomized intervention study demonstrated improved glycaemic control and reduced large for gestational age in women with Type 1 and Type 2 diabetes [21]. More widespread use of continuous glucose monitoring, along with increased access to structured education, insulin pump therapy (available to only 10% women in this cohort) and closed-loop insulin delivery maybe required to improve perinatal outcomes in Type 1 diabetes [24].

An unexpected but nonetheless intriguing finding was the association between maternal social disadvantage and large for gestational age, independent of glycaemic control and obesity. Almost two decades ago, the Diabetes in Early Pregnancy Study demonstrated that 1-h postprandial glucose levels were closely correlated with large for gestational age [25]. In this cohort, all women with Type 1 diabetes and 90% of women with Type 2 diabetes were treated with fast-acting insulin analogues. However, insulin does not influence the absorption of glucose, which is related only to the quality and quantity of carbohydrate ingested [26]. We speculate that socially disadvantaged women may eat cheaper, more refined carbohydrates, perhaps contributing to hyperglycaemic excursions and fetal growth acceleration.

There is controversy and a lack of randomized trials regarding the role of metformin for the management of Type 2 diabetes in pregnancy [27,28]. The UK National Institute for Health and Clinical Excellence (NICE) guidelines recommend that metformin may be continued throughout pregnancy if the benefits to glycaemic control outweigh any potential harm [29]. In this study, more than half the women with Type 2 diabetes used metformin at conception with no suggestion of any harmful effects. As reported by Rowan *et al.* in gestational diabetes, we were also unable to document an independent effect of metformin on glycaemic control and/or perinatal morbidity in Type 2 diabetes [6].

There were several strengths to the present study. Firstly, it is a near complete data set, with all pregnancies registered following the first antenatal contact. This enabled collection of potential confounding risk factors of maternal demographic, obstetric and diabetes treatment details, including pre-pregnancy glycaemic control measurements, postcodes, medication use and customized birthweight centiles. Secondly, it is a population-based cohort, including all pregnancies from a well-defined geographical region. Thirdly, the use of appropriate statistical methodology facilitated detailed multivariate analyses, providing new insights into the relationships between maternal risk factors and perinatal outcomes. Limitations include a lack of data regarding gestational weight gain, metformin use at delivery and higher rates of missing pre-conception HbA_{1c} data in women with Type 2 diabetes. Also, we cannot determine what proportion of neonatal care admissions were related to hypoglycaemia.

In summary, our study demonstrates that glycaemic control is the most important risk factor for congenital malformation, perinatal morbidity and perinatal mortality in women with Type 1 and Type 2 diabetes. It confirms the disappointingly poor perinatal outcomes of women with Type 1 diabetes, but provides encouragement, suggesting reduced rates of large for gestational age, preterm delivery and neonatal care in women with well-controlled Type 2 diabetes. An intriguing finding, which warrants further investigation, is the association between large for gestational age and social disadvantage, suggesting that more targeted nutritional support may be warranted for women living in disadvantaged areas.

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Table 1
Maternal characteristics data of the EASIPOD cohort broken down by type of diabetes

	Type 1 <i>n</i> = 408	Type 2 <i>n</i> = 274	<i>P</i> -value
Demographic data			
Age, years			
Median (10th–90th centile)	30 (21–38)	34 (26–40)	< 0.0001
Parity			< 0.0001
0	206 (50.6%)	84 (30.7%)	
1	112 (27.5%)	61 (22.3%)	
2	54 (13.3%)	52 (19.0%)	
3	35 (8.6%)	77 (28.1%)	
Ethnicity			
Caucasian	391 (95.8%)	164 (59.9%)	< 0.0001
Asian	12 (2.9%)	91 (33.2%)	
Other	5 (1.2%)	19 (6.9%)	
Social deprivation	<i>n</i> = 374	<i>n</i> = 271	
Quintile 1 (least deprived)	63 (16.8%)	31 (11.4%)	0.0004
Quintile 2	60 (16.0%)	33 (12.1%)	
Quintile 3	95 (25.4%)	44 (16.2%)	
Quintile 4	85 (22.7%)	52 (19.2%)	
Quintile 5 (most deprived)	101 (27.0%)	111 (41.0%)	
Weight	<i>n</i> = 380	<i>n</i> = 248	
Weight at booking, kg			
Median (10th–90th centile)	68.0 (56.0–86.9)	87.2 (62.8–117.9)	< 0.0001
BMI at booking, kg/m ²			
Median (10th–90th centile)	25.2 (21.4–31.8)	32.4 (24.1–42.4)	< 0.0001
Normal (BMI 24.9)	175 (46.1%)	28 (11.3%)	
Overweight (BMI 25–29.9)	141 (37.1%)	52 (21.0%)	
Obese (BMI 30)	64 (16.8%)	168 (67.7%)	
Diabetes status	<i>n</i> = 408	<i>n</i> = 274	
Diabetes duration, years			
Median (10th–90th centile)	13 (4–27)	3 (1–9)	< 0.0001

	Type 1	Type 2	P-value
Maternal complications			
Retinopathy	119 (29.2%)	14 (5.1%)	< 0.0001
Nephropathy	9 (2.2%)	7 (2.6%)	1.0
Neuropathy	11 (2.7%)	2 (0.7%)	0.1
Glycaemic control			
HbA _{1c} pre-pregnancy *			
Median (10th–90th centile)	63 mmol/mol (48–98) 7.9% (6.5–11.1)	52 mmol/mol (39–86) 6.9% (5.7–10.0)	< 0.0001
HbA _{1c} at first contact			
Median (10th–90th centile)	60 mmol/mol (44–85) 7.6% (6.2–9.9)	51 mmol/mol (38–75) 6.8% (5.6–9.0)	< 0.0001
HbA _{1c} 53 mmol/mol (7.0%)	89/268 (33.2%)	95/165 (57.6%)	
HbA _{1c} 1st trimester, %			
Median (10th–90th centile)	57 mmol/mol (43–81) 7.4% (6.1–9.6)	51 mmol/mol (38–69) 6.8% (5.6–8.5)	< 0.0001
HbA _{1c} 2nd trimester, %			
Median (10th–90th centile)	50 mmol/mol (39–66) 6.7% (5.7–8.2)	42 mmol/mol (33–54) 6.0% (5.2–7.1)	< 0.0001
HbA _{1c} 3rd trimester, %			
Median (10th–90th centile)	50 mmol/mol (38–65) 6.7% (5.6–8.1)	44 mmol/mol (33–56) 6.2% (5.2–7.3)	< 0.0001
Diabetes therapy at conception			
Diet alone	0 (0.0%)	73 (26.6%)	
Insulin †	408 (100%)	76 (27.7%)	
Sulphonylurea	0 (0.0%)	16 (5.8%)	
Metformin	13 (3.2%)	152 (55.5%)	
Metformin alone	0	120	
Metformin and insulin	13	32	
Gliatzone	0 (0.0%)	22 (8.0%)	
Pregnancy preparation			
Planned pregnancy	212/382 (55.5%)	119/244 (48.8%)	0.1
Pre-conceptual counselling	218/406 (53.7%)	86/269 (32.0%)	< 0.0001
Pre-pregnancy care	127/405 (31.4%)	53/271 (19.6%)	0.0009

	Type 1	Type 2	P-value
Folic acid pre-conception	181/372 (48.7%)	87/231 (37.7%)	0.009
ACE inhibitor at conception	6 (1.5%)	20 (7.3%)	0.0002
Statin therapy at conception	7 (1.7%)	32 (11.7%)	< 0.0001
Gestational age at booking, week			
Median (10th—90th centile)	7.1 (4.7–12.7)	7.9 (5.0–14.2)	0.05
Booked before 8/40	222/369 (60.2%)	132/257 (51.4%)	
Smoking status at conception			
Non-smoker	288 (72.0%)	210 (78.1%)	0.1
Ex-smoker	35 (8.8%)	14 (5.2%)	
Current smoker	77 (19.3%)	45 (16.7%)	

EASIPD, East Anglia Study Group for Improving Pregnancy Outcomes in Women with Diabetes.

* Pre-pregnancy HbA1c levels were available for 295/408 (72.3%) women with Type 1 and 146/274 (53.3%) women with Type 2 diabetes.

[†] At delivery, 207/231 (89.6%) women with Type 2 diabetes were treated with insulin.

Table 2
Obstetric and perinatal outcomes of the EASIPD cohort broken down by type of diabetes

	Type 1	Type 2	P-value
Obstetric outcome *	n = 397	n = 270	
Miscarriage	53 (13.3%)	46 (17.0%)	0.4
Termination	21 (5.3%)	4 (1.5%)	
TOP fetal abnormality	7	2	0.5
TOP non-diabetes associated	18	2	
Pre-eclampsia	31 (7.8%)	14 (5.2%)	0.3
Delivery †	n = 323	n = 220	
Type of delivery			
SVD including instrumental	118 (36.5%)	107 (48.6%)	0.006
LSCS	205 (63.5%)	113 (51.4%)	
Planned LSCS	96 (29.7%)	55 (25.0%)	0.8
Emergency LSCS	109 (33.7%)	58 (26.4%)	
Gestational age at delivery, weeks ‡			
Median (10th–90th centile)	37.4 (34.0–38.6)	38.1 (35.6–39.3)	< 0.0001
Perinatal morbidity			
Prematurity ‡	n = 322	n = 217	
Premature delivery < 37 weeks	120 (37.1%)	38 (17.5%)	< 0.0001
Early premature delivery < 34 weeks	23 (7.1%)	8 (3.7%)	0.1
Infant birthweight centiles §	n = 308	n = 210	
LGA 90th centile	163 (52.9%)	79 (37.6%)	0.0008
Extreme LGA 97.7	110 (35.7%)	54 (25.7%)	0.02
SGA 10th centile	15 (4.9%)	24 (11.4%)	0.009
Neonatal care ¶	n = 317	n = 218	0.001
Hone birth	1 (0.3%)	0 (0.0%)	
Post-natal ward	130 (41.0%)	127 (58.3%)	
Transitional	49 (15.5%)	26 (11.9%)	
SCBU	106 (33.4%)	54 (24.8%)	

	Type 1	Type 2	P-value
NICU	31 (9.8%) <i>n</i> = 330	11 (5.0%) <i>n</i> = 222	
Serious adverse outcome **			
Malformation	14 (42/1000)	9 (41/1000)	0.9
Stillbirth	5 (15/1000)	2 (9/1000)	0.8
Neonatal death	3 (9/1000)	0 (0/1000)	0.4
Perinatal mortality	8 (24/1000)	2 (9/1000)	0.3
Serious adverse outcome—malformation (± TOP), stillbirth or neonatal death	22 (67/1000)	11 (50/1000)	0.5

EASIPD, East Anglia Study Group for Improving Pregnancy Outcomes in Women with Diabetes; LGA, large for gestational age; LSCS, lower segment Caesarean section; NICU, neonatal intensive care unit; SCBU, special care baby unit; SVD, spontaneous vaginal delivery; TOP, termination of pregnancy.

* All pregnancies in the database (686), excluding four with diabetes of classes other than Type 1 or Type 2, 11 twin pregnancies (seven Type 1, four Type 2) and women who transferred out of the area for delivery (four).

† All Type 1 and Type 2 singleton pregnancies, excluding spontaneous miscarriages (99) and terminations (25).

‡ All Type 1 or Type 2 singleton pregnancies resulting in live births, excluding those for whom gestational age at delivery data were missing (four).

§ All Type 1 or Type 2 singleton pregnancies resulting in live births, excluding those for whom birthweight centile data were missing (18).

¶ All Type 1 or Type 2 singleton pregnancies resulting in live births, excluding one infant in whom care level was not recorded.

** All Type 1 or Type 2 singleton pregnancies resulting in live births, stillbirths or termination for congenital malformation, excluding women who transferred out of the area (four).