

Characteristics and outcomes of pregnant women with type 1 and type 2 diabetes: national population based 5-year cohort study

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Running title: Pregnancy outcomes in women with diabetes

Word count: main text 3500 excluding figure legends, abstract 300

Figures: 5, Tables: 2

Electronic Supplementary Materials; 12 (4 Figures, 8 Tables)

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Abstract

Background: Our aim was to identify and compare modifiable risk factors associated with adverse pregnancy outcomes in women with type 1 and type 2 diabetes and to identify effective maternity clinics.

Methods: We included 17,375 pregnancies in 15,290 women with diabetes in a population-based cohort study across 172 maternity clinics in England, Wales and the Isle of Man. Obstetric complications (preterm delivery, large birthweight) and adverse pregnancy outcomes (congenital anomaly, stillbirth, neonatal death) were obtained for pregnancies completed between 01 January 2014 and 31 December 2018. We assessed associations between modifiable (glycaemia, obesity, clinic) and non-modifiable risk factors (age, deprivation, ethnicity) with pregnancy outcomes.

Results: Of 17,375 pregnancies, 8,690 (50.0%) were in women with type 1 and 8,685 (50.0%) in women with type 2 diabetes. The rates of preterm delivery (42.5% type 1, 23.4% type 2), and large birthweight (52.2% type 1, 26.2% type 2) were higher in type 1 diabetes ($p < 0.001$). The prevalence of congenital anomaly (44.8/1000 type 1, 40.5/1000 type 2; $p = 0.175$), and stillbirth (10.4/1000 type 1, 13.5/1000 type 2; $p = 0.072$) did not differ but neonatal death rates (7.4/1000 type 1, 11.2/1000 type 2; $p = 0.013$) were higher in type 2 diabetes. Independent risk factors for perinatal death were third trimester HbA1c > 48 mmol/mol (OR 3.06, 95% CI 2.16 to 4.33), living in the highest deprivation quintile (OR 2.29 95% CI 1.16 to 4.52) and having type 2 diabetes (OR 1.65 95% CI 1.18 to 2.31). Variations in glycaemia and large birthweight were associated with maternal characteristics (diabetes duration, deprivation, BMI) without substantial differences between clinics.

Interpretation: Our data highlight persistent adverse pregnancy outcomes in type 1 and type 2 diabetes. Maternal glycaemia and obesity are the key modifiable risk factors. No clinics were achieving appreciably better outcomes, suggesting that healthcare system changes are needed

across all clinics.

Introduction

As the prevalence of diabetes continues to rise, pregnancies complicated by maternal diabetes are becoming an increasing concern. The incidence of both gestational diabetes and pregnancy complicated by type 1 or type 2 diabetes has doubled, affecting almost one in ten pregnant women by 30 years of age (1). Increases of 33-44% in pregnancies complicated by type 1 diabetes and of 90-111% in pregnancies complicated by type 2 diabetes are reported in Northern Europe (2, 3). Pregnancies complicated by pre-existing diabetes are associated with preterm delivery and birthweight extremes as well as increased rates of congenital anomaly, stillbirth, and neonatal death (4-6).

Previous studies have documented the pregnancy outcomes associated with type 1 and type 2 diabetes (1, 2, 4-9). Pregnant women with type 1 diabetes have higher glucose levels than those with type 2 diabetes, and higher associated rates of preterm births and large birthweight babies, most likely attributable both to glycaemia and body mass index (BMI) (7). Pregnant women with type 2 diabetes are older, with higher rates of obesity, ethnic diversity, and deprivation compared to women with type 1 diabetes, but they also have lower glucose levels, fewer preterm births, and fewer large birthweight babies (10). Nonetheless, adverse pregnancy outcomes (congenital anomaly, stillbirth, neonatal death) occur at least equivalently, in women with type 1 and type 2 diabetes (2, 6, 11).

The different contributions of risk factors to obstetric complications and adverse pregnancy outcomes in women with type 1 and type 2 diabetes are unclear. It is also unknown whether some maternity clinics more successfully achieve antenatal glucose targets and optimal pregnancy outcomes, independent of confounding variables (10). Here we report the first five

years of data from the National Pregnancy in Diabetes (NPID) audit, encompassing over 17,000 pregnancies in women with diabetes. Our aim was to identify and compare modifiable risk factors associated with type 1 and type 2 diabetes pregnancy outcomes in a large national cohort and to identify particularly effective maternity clinics.

Methods

Data sources

All National Health Service (NHS) maternity units in England, Wales and the Isle of Man providing antenatal diabetes care are expected to participate in the annual NPID audit (<http://digital.nhs.uk/npid>). Healthcare professionals at each maternity clinic completed web-based manual data entry forms (which introduces a risk of data entry error) for all pregnant women with pre-existing diabetes (ESM 1). Remaining data items were collected by data linkage with other systems (Hospital Episodes Statistics data, Patient Episode Database for Wales, Core National Diabetes Audit).

The information leaflet and consent forms used met the Health Research Authority requirements for clinical audit and research ethics approval was not required. The requirement for individual women to provide written informed consent was removed in England from 2018, because the legal basis for the National Diabetes Audit data collection and linkage in England became a Direction from NHS England to NHS Digital according to section 254 of the Health and Social Care Act (HSCA) for England 2012. Individual written consent is still required in Wales.

Patient and Public Involvement

Patients and the public were involved in the design and conduct of the audit, development and agreement of the statistical analyses plan and interpretation and dissemination of results.

Study population, observation period and outcomes

Our study population included women with pre-existing type 1 and type 2 diabetes who completed a pregnancy between 1st January, 2014, and 31st December, 2018. We defined pre-existing diabetes as diabetes clinically diagnosed before pregnancy and excluded women with monogenic diabetes and those who presented with diabetes first recognised during pregnancy. We defined gestational age according to the estimated date of delivery based on ultrasound assessment at 12 weeks gestation. We categorised births before 37 weeks gestation as preterm. Birthweight was adjusted for maternal BMI, ethnicity, neonatal sex and gestational age for singleton pregnancies using customised centiles with large and small for gestational age (LGA, SGA) defined as birthweight centile >90th and <10th centile respectively (Gestation Related Optimal Weight (GROW) centile tool v8 0.4 (UK) 2019 Gestation Network)(12).

Major and minor congenital anomalies were based on the ICD10 codes identified prior to hospital discharge. We calculated the congenital anomaly rate as the number of offspring with one or more anomalies divided by the number of livebirths, terminations, fetal losses after 20 weeks. We defined stillbirth as fetal loss occurring after 24 weeks gestation, and neonatal death as death of a liveborn infant up to 28 days after delivery.

Definitions of exposures

Maternal age was grouped as 15-24 years, 25-34 years, 35-44 years and age >45 years. Self-reported ethnicity was classified as White, Mixed, Asian, Black, Unknown, Other or not available (N/A). Social deprivation was based on an index of multiple deprivation score for

women whose postcode details were recorded in the National Diabetes Audit (13). Diabetes duration was categorised as <1 year, 1-4 years, 5-9 years, 10-14 years and >15 years. Maternal body mass index (BMI) was based on the first recorded weight in pregnancy and grouped as <18.5 kg/m², 18.6-24.9 kg/m², 25-29.9 kg/m², 30-34.9 kg/m², 35-39.9 kg/m², and >40 kg/m². Antenatal glucose measurements were obtained from the first and last glycated haemoglobin (HbA_{1c}) values recorded during pregnancy. HbA_{1c} was measured in routine care settings using IFCC standard assays. Target glycaemic attainment was defined as HbA_{1c} <48mmol/mol (6.5%), in accordance with National Institute for Health and Clinical Excellence (NICE) guidelines (14). We considered 5mg folic acid taken before conception, gestational age <10 weeks at first antenatal contact, and *not taking* potentially harmful medications (Angiotensin Convertase (ACE) Inhibitor, Angiotensin-II Receptor Blocking (ARB), statins) as markers of pre-pregnancy care.

Statistical analysis

In this national observational study, the sample size was governed by the incidence of pregnancies complicated by diabetes, so no formal power calculations were performed. The statistical analysis plan was agreed by the NPID advisory group. The hypothesis of interest was to determine the contribution of modifiable risk factors (HbA_{1c} levels, BMI, pre-pregnancy care, maternity clinic attended) to pregnancy outcomes after adjustment for confounding maternal characteristics (age, ethnicity, deprivation, diabetes type and duration, co-morbidities). We also explored the impact of clinic-to-clinic variations on glycaemic attainment and obstetric complications (preterm delivery, large birthweight) to identify whether there were any particularly effective maternity clinics.

When examining obstetric complications and adverse pregnancy outcomes (congenital anomaly, stillbirth, neonatal death), we used all data collected during the 5-year study period. For perinatal deaths, the regression model included diabetes type and duration, maternal age, BMI, deprivation quintile, first trimester HbA_{1c}, folic acid, potentially harmful medications and third trimester HbA_{1c}. For congenital anomaly, third trimester HbA_{1c} was omitted. We ran separate models for type 1 and type 2 diabetes where applicable and only factors which were statistically significant in univariate analyses were retained in multivariate analyses. Because neonatal deaths may have been underreported in 2014, a post hoc analysis compared neonatal death rates in type 1 and type 2 diabetes during 2015-2018.

For exploring the impact of maternity clinic attended, we used data collected during 2017-2018 when audit participation was stable (166 clinics in 2017, 164 clinics in 2018). This ensured as homogenous a group as possible. For data protection of potentially sensitive information in the clinic-to-clinic regression models, we excluded clinics with fewer than five outcomes.

Variables which were not normally distributed are given as median (interquartile range, IQR) while normally distributed variables are given as mean (SD). Univariate analyses comparing the proportions between groups were performed using z-tests and t-tests for comparing continuous variables. We used SAS EG v7.1 for analyses and Poisson distribution to obtain 95% confidence intervals for the rate and prevalence ratios.

Results

Participation

The number of National Health Services (NHS) maternity clinics who participated across the five years ranged from 150 to 172. There was some variation in participating clinics with 13 clinics submitting data for the first time in 2017-18, and an increase in pregnancies reported during 2017 and 2018, both before and after requirement for written consent was removed in England. Data on 17,375 diabetes pregnancies, including 700 congenital anomalies, 345 perinatal deaths (195 stillbirths, 150 neonatal deaths) in 15,290 pregnant women with diabetes are included (Table 1).

Maternal characteristics

Half of the pregnancies ($n=8685$) were in women with type 2 diabetes (Table 2). As expected, women with pregnancies complicated by type 2 diabetes were older, and had a shorter duration of diabetes. Compared to women with type 1 diabetes, they were more likely to live in areas of deprivation, be of Asian or Black ethnicity and be overweight or obese. Among women with type 1 diabetes, about 20% more pregnancies than expected (according to general population conception statistics) occurred in women with greater deprivation. The socioeconomic gradient in conceptions was particularly pronounced in women with type 2 diabetes, with more than 40% living in the most deprived and less than 6% in the least deprived quintile.

Pregnant women with type 2 diabetes presented for antenatal care approximately two weeks later than women with type 1 diabetes, and had higher rates of treatment with antihypertensive and lipid-lowering medications and lower rates of 5mg preconception folic acid. They also had lower HbA_{1c} and were more likely than women with type 1 diabetes to achieve the NICE glycaemic target of HbA_{1c} <48mmol/mol (6.5%). Almost two thirds of women with type 2 diabetes (64.9%) were taking metformin in early pregnancy (ESM 2). There were no changes

in folic acid use but there was a reduction in potentially harmful medication usage in women with type 2 diabetes over the five-year study period (ESM 3). Insulin pump therapy was used by 1890 (22.4%) women with type 1 diabetes, increasing from 19.3% in 2014 to 24.8% in 2018 (ESM 4). There were no changes in maternal glycaemia over the five-year study period (ESM 5).

Obstetric and neonatal complications

Rates of preterm births, large for gestational age babies and neonatal care admissions were all higher in type 1 diabetes, while rates of small for gestational age babies (5.4% type 1, 14.1% type 2; $p < 0.001$) were higher in type 2 diabetes. In type 1 diabetes, the rates of preterm births and large for gestational age babies also increased over the five-year study period (ESM 6).

Adverse pregnancy outcomes

Women with pregnancies complicated by type 2 diabetes had a comparable stillbirth rate (10.4/1000 type 1, 13.5/1000 type 2; $p = 0.072$) and a significantly higher neonatal death rate (7.4/1000 type 1, 11.2/1000 type 2; $p = 0.013$) (Table 1, Figure 1). The increased neonatal death rate in type 2 diabetes persisted after excluding data from 2014; (8.1/1000 type 1, 11.7/1000 type 2 in 2015-2018; $p = 0.036$). There were 700 congenital anomalies (ESM 7) with no difference in prevalence (44.8/1000 type 1, 40.5/1000 type 2; $p = 0.175$) between type 1 and type 2 diabetes. Women with type 2 diabetes had higher rates of perinatal death across all third trimester HbA1c categories below 86mmol/mol (Figure 2); HbA1c <43mmol/mol (0.6% type 1, 0.9% type 2), HbA1c 44-52mmol/mol (1.2% type 1, 2.7% type 2), HbA1c 53-63mmol/mol (1.7% type 1, 4.0% type 2), HbA1c 64-74mmol/mol (1.7% type 1, 4.9% type 2), HbA1c 75-85mmol/mol (8.3% type 1, 10.0% type 2).

Among the entire cohort, independent risk factors for perinatal death were third trimester HbA_{1c} \geq 48mmol/mol (OR 3.06, 95% CI 2.16-4.33), living in the highest deprivation quintile (OR 2.29 95% CI 1.16-4.52) and having type 2 diabetes (OR 1.65 95% CI 1.18-2.31) (ESM 8). When examined according to type of diabetes, only third trimester HbA_{1c} \geq 48mmol/mol (6.5%) remained significantly associated with perinatal death in both type 1 (OR 2.47 95% CI 1.49-4.08) and type 2 diabetes (OR 3.93 95% CI 2.51-6.16).

For congenital anomaly, only first trimester HbA_{1c} \geq 48mmol/mol (OR 1.70 95% CI 1.35-2.14) and not taking 5mg preconception folic acid (OR 1.31 95% CI 1.08-1.58) were significant independent risk factors among the entire cohort. When examined by type of diabetes, an above target HbA_{1c} remained significantly associated with congenital anomaly in type 1 (OR 1.79, 95% CI 1.2-2.7) and type 2 diabetes (OR 1.64, 95% CI 1.23-2.21) with not taking folic acid (OR 1.30, 95% CI 1.02-1.65) also significant in type 1 diabetes.

Variation in HbA_{1c}

Variation in target HbA_{1c} attainment in early pregnancy was more dependent on maternal characteristics than maternity clinic attended. Specifically, after adjustment for maternal age, ethnicity, deprivation, BMI, type and duration of diabetes, we found minimal variation between clinics, with most falling within the expected distribution (Figure 3). In type 1 diabetes, women with target HbA_{1c} were older (35-44yrs) and had shorter diabetes duration (Figure 4, ESM 9). Younger women (<24yrs), with higher deprivation, longer diabetes duration, and higher BMI were less likely to achieve target HbA_{1c}. In women with type 2 diabetes, longer diabetes duration, higher BMI, deprivation and Black or Asian ethnicity were associated with higher HbA_{1c}.

Likewise, HbA_{1c} in late pregnancy was more strongly associated with maternal characteristics than maternity clinic attended (Figure 3). First trimester HbA_{1c} was the most important predictor for third trimester HbA_{1c} in type 1 and type 2 diabetes, with diabetes duration also contributing. There was a direct association between higher maternal BMI and above target third trimester HbA_{1c} in type 1 diabetes (ESM 10).

Variation in obstetric complications

We found some differences across clinics in the rates of preterm births, with six clinics falling two standard deviations above the expected average rates (Figure 5). Factors associated with preterm birth in type 1 diabetes were younger maternal age (<24yrs), deprivation, longer diabetes duration and higher HbA_{1c} (ESM 11). Higher first and third trimester HbA_{1c} and longer diabetes duration were also associated with preterm birth in type 2 diabetes. Black and Asian women were more likely to have term births.

Variation in large for gestational age birthweight was strongly associated with maternal characteristics with no evidence for substantial variation between clinics (Figure 5). Factors associated with having a large birthweight baby in type 1 diabetes were not taking potentially harmful medications (reflecting less maternal comorbidity) and higher first and third trimester HbA_{1c} (ESM 12). Being older (35-44 years) and presenting for antenatal care after 10 weeks gestation were associated with reduced risk for large birthweight. An above target HbA_{1c}, especially during the third trimester, was associated with large birthweight in type 2 diabetes, with older women less likely to have a large birthweight baby compared to younger women.

Discussion

In pregnant women with type 2 diabetes, we found higher than expected rates of perinatal death. Third trimester HbA_{1c} was the dominant risk factor, both in women with type 1 and type 2 diabetes. In pregnant women with type 1 diabetes, above target HbA_{1c} was common and increased with maternal obesity, while rates of preterm births and large birthweight babies were elevated and rising. We did not identify any clinics that were significantly more effective in achieving optimal glycaemic or neonatal birthweight outcomes.

To our knowledge, this is the largest, most detailed contemporary dataset in pregnant women with diabetes. It included 200 perinatal deaths in type 2 diabetes (110 stillbirths, 90 neonatal deaths), and 145 (85 stillbirths, 60 neonatal deaths) in type 1 diabetes. Previous studies included fewer pregnant women, especially those with type 2 diabetes (6). A Scottish study recently reported pre-pregnancy HbA_{1c} and BMI as key risk factors associated with stillbirth in type 2 diabetes. We found that after adjusting for these and other risk factors, an above target third trimester HbA_{1c} was associated with a four-times increased risk of perinatal death in type 2 diabetes. We also found that across all third trimester HbA_{1c} categories, pregnant women with type 2 diabetes had higher rates of perinatal death compared to women with type 1 diabetes.

Studies in general maternity populations have demonstrated that stillbirth rates are increased at birthweight extremes, and that growth-restricted pregnancies have the highest risk (15-17). Scottish data confirmed these findings in diabetes pregnancies, describing a six-times increased risk of stillbirth in small and a two-times increased risk in large birthweight babies (18). The higher rates of small for gestational age babies in type 2 diabetes likely contributes to the higher odds of perinatal death in our cohort.

Large birthweight remains the commonest complication of pregnancy in type 1 and type 2 diabetes. Consistent with Scottish data, where the large birthweight rate increased in type 1 diabetes during 1998-2013, we also found a temporal increase over the five years from 2014-2018 (2). The reasons for this are unclear. Although we confirm the known association with higher HbA_{1c}, we found no association with obesity, possibly because we used customised growth centiles, and because of the interaction between higher BMI and glycaemia. Interestingly, we found no glycaemic deterioration as reported in other cohorts (19). Women *not taking* antihypertensive or lipid lowering treatments had an increased risk, suggesting that in addition to glycaemia, maternal co-morbidities which influence placental vascular function are important. We also found that no maternity clinics were significantly more effective for achieving optimal birthweight outcomes.

Potentially modifiable risk factors

Surprisingly few women with type 2 diabetes were taking insulin (18%) or 5mg folic acid (22%) in early pregnancy, suggesting that despite two decades of adverse pregnancy outcomes, type 2 diabetes is still considered a less serious condition. Almost two thirds (65%) of women with type 2 diabetes were taking metformin, demonstrating healthcare engagement but missed opportunities for improving pregnancy preparation. Previous studies have confirmed that pre-pregnancy programmes are effective, but that fewer women with type 2 diabetes attend (20, 21). Qualitative studies suggest that unhelpful beliefs about age, obesity and fertility need to be addressed for more effective implementation of pre-pregnancy care in women with type 2 diabetes (22).

Raised HbA_{1c} was associated with higher rates of adverse outcome in both type 1 and type 2 diabetes pregnancies. A third of women with type 1 diabetes were overweight, with almost a

quarter obese, which was adversely associated with glycaemic attainment. Women with type 1 diabetes may require additional dietary and psychosocial support to optimise their weight in order to achieve the pregnancy glucose targets. Younger women with type 1 diabetes (aged 15-24 years) were most at risk for entering pregnancy with higher HbA_{1c}, suggesting unplanned pregnancies and implying that greater attention to contraception provision across paediatric and young adult diabetes services may yield benefit.

In type 2 diabetes, the modifiable risk factors for higher HbA_{1c} included duration of diabetes and maternal obesity, both of which can be mitigated by intensive dietary interventions (23, 24). Many women with type 2 diabetes (between one third and half) will have experienced previous pregnancies complicated by gestational diabetes (25). There is an urgent need to accelerate diabetes prevention programmes that proactively engage women with gestational diabetes (26).

The lack of clinic-to-clinic variation in glycaemic attainment suggests that changes to maternity diabetes care are required in order for all clinics to achieve optimal glycaemia across a broader range of women. Interventions such as the introduction of continuous glucose monitoring may improve antenatal glucose levels and neonatal health outcomes in type 1 diabetes (27). Many maternal characteristics (younger age, higher deprivation, longer diabetes duration) associated with higher HbA_{1c} are not modifiable, so targeting dietary, educational and technological resources, such as automated insulin delivery, towards women with the highest risk profiles may be required (28). Women with type 2 diabetes need culturally appropriate pre-pregnancy and antenatal care. In addition, input from multidisciplinary obesity services as well as tighter glucose targets, potentially achievable using continuous glucose monitoring systems, may be

applicable (29). Further evaluation of the impact of metformin on small for gestational age birthweight and stillbirth is needed (30).

A major strength is the identification of a detailed, national cohort of pregnant women with diabetes with high case ascertainment across UK maternity units. The large sample which included 345 perinatal deaths, yielded robust estimates for serious adverse pregnancy outcomes. In addition, data from >150 maternity clinics allowed a depth of analysis not previously possible, including the development of national average rates for glycaemic attainment and obstetric complications. Our dataset variable list is limited to key pregnancy outcomes and lacks data on diabetes complications. We acknowledge data quality issues of ‘real-world’ clinical data especially for diabetes diagnosis and medication usage, however this affects only a small number (1.3%) of pregnancies and is unlikely to impact our results. Also, we cannot determine the impact of the continued requirement for consent in Wales, but do not expect this to impact our findings. Other limitations include data missingness with fewer HbA1c measurements in type 2 diabetes pregnancies (>80% type 1, 72% type 2), no information on gestational weight gain and of observational analyses, which preclude causal inferences.

Our findings have implications for research, healthcare policy and clinical practice. Our results can serve as a reference point from which to judge the effectiveness of future interventions to optimise pregnancy outcomes in type 1 and type 2 diabetes. They highlight ongoing, unchanged adverse pregnancy outcomes in type 1 diabetes and increased perinatal deaths in type 2 diabetes. Improving pregnancy outcomes is a shared challenge which requires better diabetes healthcare system integration across primary care, paediatric and young adult clinics as well as adult diabetes, obesity and maternity services.

Research in Context

Evidence before this study

We searched PubMed for articles published before July 30, 2020, without restriction on language or start date. We included the search terms (“Diabetes Mellitus” OR “Diabetes”), AND “pregnancy”, OR “pregnancy in diabetics”, AND “congenital anomaly”, AND (“perinatal death”) AND (“stillbirth”) AND (“neonatal death”). Previous studies were conducted 15-20 years ago and included far fewer pregnant women, especially those with type 2 diabetes. The UK Confidential Enquiry into Maternal and Child Health (CEMACH) conducted during 2002-03 documented a threefold increase in perinatal mortality and a twofold increase in the congenital anomaly rate in women with diabetes. They described 25 perinatal deaths (19 stillbirths, 6 neonatal deaths) in 652 women with type 2 diabetes, with comparable rates in women with type 1 and type 2 diabetes. They noted high levels of ethnic diversity, obesity, deprivation and poor preparation for pregnancy in women with type 2 diabetes. A Scottish study conducted during 1998-2016 described 37 stillbirths in 1614 women with type 2 diabetes, again highlighting the importance of pre-pregnancy care.

Added value of this study

Our national cohort of 17,375 pregnancies described the glycaemic status and pregnancy outcomes in 15,290 women, half of whom had type 2 diabetes. In pregnant women with type 2 diabetes, we found higher than expected rates of perinatal death. Third trimester HbA1c > 48mmol/mol (6.5%) was associated with a four-times increased risk for perinatal death. Across all third trimester HbA1c categories, pregnant women with type 2 diabetes had higher rates of perinatal death compared to women with type 1 diabetes suggesting that more vigilant attention to antenatal glucose levels is needed in type 2 diabetes. In pregnant women with type 1 diabetes, HbA1c levels above 48mmol/mol (6.5%) increased with maternal obesity, while rates of preterm births and large birthweight babies were elevated and rising. Glycaemic attainment was associated with maternal obesity as well as non-modifiable characteristics (maternal age, deprivation, diabetes duration) but not by maternity clinic attended.

Implications of all the available evidence

Our data highlight persistent adverse pregnancy outcomes in type 1 and type 2 diabetes and higher perinatal deaths in type 2 diabetes. They reinforce the critical importance of maternal glycaemia as the key modifiable risk factor and the negative impact of obesity in women with both types of diabetes. Improving pregnancy outcomes is a shared challenge which likely requires better diabetes healthcare system integration across primary care, paediatric and young adult clinics as well as adult diabetes, obesity and maternity services plus new systems for optimising glycaemia.

Abbreviations: Angiotensin Converting Enzyme (ACE), Body Mass Index (BMI), Gestation Related Optimal Weight (GROW), Interquartile Range (IQR), Large for Gestational Age (LGA), National Health Services (NHS), National Pregnancy in Diabetes (NPID),

Acknowledgements: The authors are extremely grateful to all the women who consented to participate and to local antenatal diabetes health care teams for their support with data entry. We are also grateful to Alex Berry (Diabetes UK, London, UK) for patient and professional input, NPID engagement activities, and to all members of the NPID advisory group (Alex Berry, Carla Howgate, Sophie Colling, Matt Curley, Angela Pinnock, Lucy Shonegeval, Nickey Tomkins, Liz Draper, Jenny Kurinczuk, Jane Hawdon, Richard Holt, Di Todd, Mike Maresh, Nick Lewis-Barned) for their past and ongoing support.

Funding: The National Pregnancy in Diabetes audit (NPID) is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit (NCA) programme funded by NHS England and the Welsh government. The audit is prepared in collaboration with NHS Digital and supported by Diabetes UK and Public Health England.

Duality of Interest: HRM sits on a scientific advisory board for Medtronic (insulin pump manufacturer). The authors declare that there is no duality of interest associated with this manuscript.

Author Contribution: HRM, CH, JOK developed the study concept and design. JOK and PK analysed the data. HRM drafted the manuscript with key input from JOK and BY. All authors critically reviewed the manuscript for important intellectual content and gave final approval for publication. HRM is the guarantor of this work.

Prior Presentation: Parts of these data were presented at the National Pregnancy in Diabetes meeting, Bristol, UK November 2019. The 2018 National Pregnancy in Diabetes Audit Report was published online October 2019.

Data Sharing: See <http://content.digital.nhs.uk/npid> for data sharing details.

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Table 1: Numbers of clinics, women, pregnancies and babies during 2014-2018

	2014	2015	2016	2017	2018
Clinics ^a	150	155	172	166	164
Women	2537	3036	3297	3840	4390
Pregnancies ^b	2553	3044	3304	3855	4400
Total pregnancy outcomes ^c	2584	3086	3356	3910	4465
Pregnancies ongoing after 24 weeks	2387	2866	3091	3545	4030
Live Births after 24 weeks	2390	2868	3108	3550	4035
Stillbirths ^d	28	37	35	40	55
Stillbirth rate per 1,000 live and stillbirths (95% CI)	12.8 (9.6-16.7)	12.2 (8.6-16.8)	10.2 (6.9-14.3)	11.7 (8.4-15.8)	13.7 (10.3-17.8)
Babies born after 24 weeks	2390	2903	3140	3590	4090
Neonatal deaths ^e	14	30	31	35	40
Neonatal death rate per 1,000 livebirths (95% CI)	7.6 (5.1-10.8)	10.0 (6.7-14.3)	10.0 (6.8-14.1)	9.6 (6.6-13.4)	10.4 (7.5-14.0)
Total registered births	2433	2908	3145	3600	4090

^aThere are a range of maternity clinics submitting data; for example in 2018 the mean number of pregnancies per clinic was 27 but there were 20 clinics with fewer than 10 pregnancies and 4 clinics with more than 80 pregnancies.

^bThere was an increase in pregnancies reported during 2017 and 2018, both before and after requirement for written consent was removed in England. Details of the data quality procedures and the number of participating clinics are available <https://files.digital.nhs.uk/79/4B7BB9/National%20Pregnancy%20in%20Diabetes%20Audit%20Report%202018%20Data%20Quality%20Statement.pdf>

^cTotal pregnancy outcomes include pregnancy loss before 24 weeks, pregnancy terminations livebirths and stillbirths. Each fetus/baby is counted so a twin pregnancy is counted as two pregnancy outcomes

^dAlthough there was an increase in the number of stillbirths from 2014-2018 there was no significant change in the overall stillbirth rate

^eWe believe that neonatal deaths were underrepresented in type 1 diabetes in 2014. When the 2014 data are excluded, there was no significant change in the overall neonatal death rate from 2015-2018

Table 2: Maternal and neonatal characteristics by diabetes type

	Type 1 diabetes ^a <i>n=8690 (50%)</i>	Type 2 diabetes <i>n=8685 (50%)</i>	<i>p</i> value
Age at delivery (years)	30 (22-37)	34 (27-41)	
Duration of diabetes (years)	13.0 (3-25)	3.0 (0-10)	
Weight at booking (kg)	70 (56.3-93.0)	85.6 (62.0-117.0)	
BMI at booking (kg/m ²)	25.9 (21.3-33.8)	32.5 (24.8-43.0)	
BMI category	<i>n=8680</i>	<i>n=8680</i>	
18.5–24.9	3640 (41.9%)	915 (10.5%)	<0.001
25–29.9	3060 (35.3%)	2125 (24.5%)	<0.001
≥30	1975 (22.8%)	5640 (65.0%)	<0.001
Ethnicity^b	<i>n=8645</i>	<i>n=8360</i>	
White	7370 (85.3%)	3610 (43.2%)	<0.001
Asian	335 (3.9%)	2980 (35.6%)	<0.001
Black	185 (2.1%)	805 (9.6%)	<0.001
Mixed	110 (1.3%)	205 (2.5%)	<0.001
Other	140 (1.6%)	240 (2.9%)	<0.001
Not stated/unknown	510 (5.9%)	520 (6.2%)	0.381
Deprivation quintile	<i>n=8220</i>	<i>n=7780</i>	
1: least deprived	1285 (15.6%)	445 (5.7%)	<0.001
2	1465 (17.8%)	740 (9.5%)	<0.001
3	1670 (20.3%)	1315 (16.9%)	<0.001
4	1790 (21.8%)	2055 (26.4%)	<0.001
5: most deprived	2010 (24.5%)	3225 (41.5%)	<0.001
Treated Hypertension	<i>n=7460</i>	<i>n=7825</i>	
	275 (3.7%)	805 (10.3%)	<0.001
Markers of pregnancy preparation	<i>n=8685</i>	<i>n=8680</i>	
5mg folic acid preconception	3830 (44.1%)	1930 (22.3%)	<0.001
ACE inhibitor/ARB	105 (1.2%)	355 (4.1%)	<0.001
Statin	130 (1.5%)	460 (5.3%)	<0.001
Gestation at first contact (weeks)	7 (4-12)	9 (5-15)	
Maternal Glycemia	<i>n=7135</i>	<i>n=6265</i>	
Early HbA _{1c} (mmol/mol)	60.0 (44.0–88.0)	51.5 (39.0–83.0)	
HbA _{1c} <48 mmol/mol (6.5%)	1135 (15.9%)	2285 (36.5%)	<0.001
Late pregnancy HbA_{1c}	<i>n=6515</i>	<i>n=5885</i>	

HbA _{1c} (mmol/mol)	50 (38–66)	42 (33–56)	
HbA _{1c} <48 mmol/mol (6.5%)	2715 (41.7%)	4335 (73.7%)	<0.001
Obstetric outcomes	<i>n</i> =7825	<i>n</i> =7815	
Gestational age at delivery (wks)	37 (34–38)	38 (35–39)	
Preterm delivery <37 ⁺⁰ weeks	3325 (42.5%)	1825 (23.4%)	<0.001
Preterm delivery <34 ⁺⁰ weeks	720 (9.2%)	395 (5.1%)	<0.001
Infant birthweight percentiles	<i>n</i> =7845	<i>n</i> =7885	
LGA >90th percentile	4095 (52.2%)	2065 (26.2%)	<0.001
SGA >10th percentile	420 (5.4%)	1115 (14.1%)	<0.001
Neonatal care admission	<i>n</i> =8060	<i>n</i> =8035	
Special care unit	2470 (30.6%)	1440 (17.9%)	<0.001
Intensive care unit	1025 (12.7%)	630 (7.8%)	<0.001
Adverse pregnancy outcome	<i>n</i> =8150	<i>n</i> =8150	
Congenital anomaly ^c	365 (44.8/1000)	330 (40.5/1000)	0.175
Stillbirth	85 (10.4/1000)	110 (13.5/1000)	0.072
	<i>n</i> =8065	<i>n</i> =8035	
Neonatal death	60 (7.4/1000)	90 (11.2/1000)	0.013

Data are presented as n (%), or *n* (*n* per 1000 births) and median (10–90th percentile) as appropriate

^aType of diabetes was clinically defined by local diabetes maternity teams. Some data quality issues were noted with 1.3% of women with type 1 diabetes not taking insulin. Details of the data quality procedures and the number of participating clinics are available <https://files.digital.nhs.uk/79/4B7BB9/National%20Pregnancy%20in%20Diabetes%20Audit%20Report%202018%20Data%20Quality%20Statement.pdf>

^bEthnicity data are obtained by data linkage with the National Diabetes Audit based on self-identified ethnicity as recorded by GP practice. Women of Asian or Black ethnicity comprised 5% of type 1 diabetes pregnancies in deprivation quintile 1 (least deprived) and 14% of those in quintile 5 (most deprived); by contrast the proportions of women of Asian or Black ethnicity with type 2 diabetes pregnancies were 38% (least deprived) and 58% most deprived).

^cIncludes major and minor congenital anomalies identified based on the ICD10 codes prior to hospital discharge.

^dThese data are applicable for singleton pregnancies. Birthweight was adjusted for maternal BMI, ethnicity, neonatal sex and gestational age for singleton pregnancies using the Gestation Related Optimal Weight (GROW) centile tool v8 0.4 (UK) 2019 Gestation Network (12). Maternal ethnicity categories included European (British, Irish, North, South, East & West European), African (North, East, Central, West & South African), Middle Eastern (Iraq, Israel, Jordan, Lebanon, Saudi Arabia, Syria, Turkey), Bangladeshi, Indian (India & Sri Lanka), Pakistani, Chinese (China, Hong Kong, Taiwan), Far East Asia (Japan, Korea, Mongolia), South East Asia (Brunei, Cambodia, Indonesia, Malaysia, Myanmar, Philippines, Thailand), Caribbean (Barbados, Cuba, Jamaica, Puerto Rico), Mixed African-European, Mixed Asian-European, Mixed Caribbean-European and other (Australasia, Americas, Asia-other).

Figure 1: Perinatal death rates in type 1 and type 2 diabetes

Top panel: Stillbirth rate per 1,000 live and stillbirths. The stillbirth rates in type 1 diabetes are unchanged during 2014-2018 but stillbirth rates in type 2 diabetes appear higher since 2016.

Bottom panel: Neonatal death rate per 1,000 livebirths. We believe that neonatal deaths may have been underrepresented in type 1 diabetes in 2014.

Figure 2: Adverse pregnancy outcome and maternal HbA1c level in pregnancies complicated by type 1 and type 2 diabetes

Top panel: Rates of congenital anomaly or perinatal death and early pregnancy HbA1c

Bottom panel: Rates of perinatal death (stillbirth and neonatal death) and late pregnancy HbA1c

The HbA1c categories are <43mmol/mol (<6.1%), HbA1c 44-52mmol/mol (6.2-6.9%), HbA1c 53-63mmol/mol (7.0%-7.9%), HbA1c 64-74mmol/mol (8.0%-8.9%), HbA1c 75-85mmol/mol (9.0-9.9%), HbA1c \geq 86mmol/mol (\geq 10%).

Figure 3: Variation between clinics in glycaemic attainment

Top panel: The proportion of women with target HbA1c in early pregnancy. The funnel plot shows the standardised ratio for first trimester HbA1c <48mmol/mol (6.5%) during 2017-2018 adjusting for maternal age, diabetes type, duration of diabetes, ethnicity, deprivation and BMI at the first antenatal appointment. Services with an expected value of 5 or fewer have been excluded. Model c statistic = 0.70

Bottom panel: The proportion of women with target HbA1c in late pregnancy. The funnel plot shows the standardised ratio for third trimester HbA1c <48mmol/mol (6.5%) during 2017-2018 adjusting for maternal age, diabetes type, duration of diabetes, ethnicity, deprivation, HbA1c and BMI at the first antenatal appointment. Services with an expected value of 5 or fewer have been excluded. Model c statistic = 0.82

Figure 4: Impact of maternal characteristics on glycaemic attainment

Odds ratios of factors associated with achieving a first trimester HbA1c of less than 48 mmol/mol (6.5%). Separate multivariate analyses were run for type 1 and type 2 diabetes

Figure 5: Variation between clinics in rates of obstetric complications

Top panel: The funnel plot shows the standardised ratio for the rate of preterm births during 2017-2018 adjusting for type and duration of diabetes, maternal age, deprivation, ethnicity, gestational age at first contact, HbA1c in early and late pregnancy, congenital anomaly and LGA. There are six clinics whose standardised ratio falls outside 2SD. Services with an expected value of 5 or fewer have been excluded. Model c statistic = 0.71.

Bottom panel: The funnel plot shows the standardised ratio for the rate of LGA babies with birthweight \geq 90th centile during 2017-2018 adjusting for maternal age, diabetes type, duration of diabetes, first and third trimester HbA1c, medications at conception and gestational age at first contact. Maternal BMI was not retained in the regression model as it did not add statistical power. Services with an expected value of 5 or fewer have been excluded. Model c statistic = 0.71