

What is already known on this topic

International studies have shown that a substantial portion of adolescents and adults with a persistent cough have evidence of a *Bordetella pertussis* infection

Parents are more likely to worry about their child's cough and want further investigations if they do not have a clear diagnosis

What this study adds

A substantial proportion of immunised school age children presenting to UK primary care with a persistent cough had evidence of a recent infection with *Bordetella pertussis*

symptoms or prevents transmission.¹⁰ However, a secure diagnosis of pertussis will allow general practitioners to give parents an indication of the likely length of cough and prevent them prescribing unnecessary drugs for asthma or referring children for further investigations.

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serology, and TH and ABB gave microbiological advice. RP did the data analysis, supervised by AH and RM-W. AH wrote the manuscript, and all authors commented on the text. AH is the guarantor.

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Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study

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Editorial by
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Abstract

Objective To provide perinatal mortality and congenital anomaly rates for babies born to women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland.

Design National population based pregnancy cohort.

Setting 231 maternity units in England, Wales, and Northern Ireland.

Participants 2359 pregnancies to women with type 1 or type 2 diabetes who delivered between 1 March 2002 and 28 February 2003.

Main outcome measures Stillbirth rates; perinatal and neonatal mortality; prevalence of congenital anomalies.

Results Of 2359 women with diabetes, 652 had type 2 diabetes and 1707 had type 1 diabetes. Women with type 2 diabetes were more likely to come from a black, Asian, or other ethnic minority group (type 2, 48.8%; type 1, 9.1%) and from a deprived area (type 2, 46.3%

in most deprived fifth; type 1, 22.8%). Perinatal mortality in babies of women with diabetes was 31.8/1000 births. Perinatal mortality was comparable in babies of women with type 1 (31.7/1000 births) and type 2 diabetes (32.3/1000) and was nearly four times higher than that in the general maternity population. 141 major congenital anomalies were confirmed in 109 offspring. The prevalence of major congenital anomaly was 46/1000 births in women with diabetes (48/1000 births for type 1 diabetes; 43/1000 for type 2 diabetes), more than double that expected. This increase was driven by anomalies of the nervous system, notably neural tube defects



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(4.2-fold), and congenital heart disease (3.4-fold). Anomalies in 71/109 (65%) offspring were diagnosed antenatally. Congenital heart disease was diagnosed antenatally in 23/42 (54.8%) offspring; anomalies other than congenital heart disease were diagnosed antenatally in 48/67 (71.6%) offspring.
Conclusion Perinatal mortality and prevalence of congenital anomalies are high in the babies of women with type 1 or type 2 diabetes. The rates do not seem to differ between the two types of diabetes.

Introduction

Pregnancy in women with diabetes is associated with an increased risk of congenital anomaly, perinatal morbidity, and mortality in their offspring. These risks have been evaluated predominantly in women with type 1 diabetes.¹⁻⁴ The incidence of both type 1 and type 2 diabetes is increasing,^{5,6} and the Confidential Enquiry into Maternal and Child Health (CEMACH) initiated a programme to assess the quality of maternity care and to examine pregnancy outcomes for women with diabetes in England, Wales, and Northern Ireland.^{7,8} Here we present perinatal mortality and congenital anomaly rates in the offspring of women with type 1 or type 2 diabetes, born between 1 March 2002 and 28 February 2003.

Methods

We defined pre-gestational diabetes as either type 1 or type 2 diabetes that had been diagnosed at least one year before the woman's estimated delivery date. Health professionals at each maternity unit filled in a notification form and questionnaire for every woman who met the criteria. The questionnaire covered demographic characteristics, type of diabetes, glycaemic control measurements, care from pre-pregnancy to the neonatal period, and outcome details up to day 28 for the baby. CEMACH regional managers coordinated data collection, validation of data, and entry on to a database.

All health professionals in England, Wales, and Northern Ireland are required to take part in confidential inquiry programmes; 231 units participated, and 2621 pregnancies were notified during the study period. We excluded 262 pregnancies that resulted in miscarriage at less than 20 weeks of gestation or termination of pregnancy for indications other than congenital anomaly.

Deprivation—We explored the relation between diabetes in pregnancy and deprivation by applying an index of multiple deprivation score.⁹ As this measure applies only to England, we excluded women resident in Wales and Northern Ireland from this exercise.

Perinatal and neonatal mortality—We compared perinatal mortality with national mortality data from the CEMACH 2002 perinatal death notifications and the Office for National Statistics.¹⁰ For definitions see bmj.com.

Congenital anomalies—We collected data on presumed congenital anomalies for live births antenatally and up to 28 days of life, for fetal losses after 20 completed weeks of gestation, and for terminations of pregnancy at any gestation. We confirmed the reported diagnoses by postmortem findings, genetic results, or correspondence.

Statistical analysis—We used Stata 8.0 for analyses. We used the Poisson distribution to obtain exact 95% confidence intervals for the rate and prevalence ratios. See bmj.com for details of methods.

Results

Of the 2359 pregnancies, 37 were twin pregnancies and two were triplet pregnancies, resulting in 2400 offspring (see bmj.com for outcomes according to gestational age).

Maternal characteristics

More than a quarter of the pregnancies were in women with type 2 diabetes (n = 652; 27.6%). Compared with the women with type 1 diabetes, women with type 2 diabetes were older at onset of diabetes (P < 0.001) and at delivery (P < 0.001), less likely to be primigravid (P < 0.001), and more likely to live in a deprived area (P < 0.001) and to come from a black, Asian, or other ethnic minority group (P < 0.001) (table 1).

Most women (1606; 68%) had a recorded measurement of glycaemic control by 13 weeks of pregnancy. Good control, defined by glycated haemoglobin (HbA_{1c}) of less than 7%, was achieved by 596 (37%) women.

Table 1 Maternal characteristics by type of diabetes. Values are numbers (percentages) unless stated otherwise

	Women with type 1 diabetes (n=1707)	Women with type 2 diabetes (n=652)
Median (IQR) age (years) at onset of diabetes	15 (9-23)	29 (25-34)
Median (IQR) age (years) at delivery	30 (26-34)	34 (30-37)
Ethnicity:		
White	1549 (90.7)	331 (50.8)
Black African	23 (1.4)	47 (7.2)
Black Caribbean	27 (1.6)	33 (5.1)
Black other	4 (0.2)	3 (0.5)
Indian	25 (1.5)	47 (7.2)
Pakistani	24 (1.4)	106 (16.3)
Bangladeshi	7 (0.4)	47 (7.2)
Chinese	1 (0.1)	2 (0.3)
Other	45 (2.6)	33 (5.1)
Not known	2 (0.1)	3 (0.5)
Multiparous	925 (54.2)	495 (75.9)
Deprivation fifth*:		
1 (least deprived)	260 (16.7)	40 (6.4)
2	288 (18.5)	66 (10.5)
3	313 (20.1)	81 (12.9)
4	307 (19.7)	145 (23.1)
5 (most deprived)	355 (22.8)	291 (46.3)
Not known	35 (2.2)	5 (0.8)
Resident in Wales or Northern Ireland	149	24

IQR=interquartile range.
 *Percentages calculated only for women resident in England.

Table 2 Maternal age adjusted stillbirth rate and perinatal and neonatal mortality in births to women with type 1 and type 2 diabetes compared with national data

	Type 1 and 2 diabetes (n=2356 live and stillbirths)		National rate* (n=620 841)	Rate ratio (95% CI)
	Number	Rate (95% CI)		
Stillbirth†	63	26.8 (19.8 to 33.8)	5.7	4.7 (3.7 to 6.0)
Perinatal death‡	75	31.8 (24.2 to 39.4)	8.5	3.8 (3.0 to 4.7)
Neonatal death‡	22	9.3 (5.2 to 13.3)	3.6	2.6 (1.7 to 3.9)

*Source for national data: CEMACH 2002.⁸
 †Rate per 1000 live births plus stillbirths.
 ‡Rate per 1000 live births.

Perinatal mortality

During the study, 63 stillbirths and 22 neonatal deaths occurred. Figures adjusted for maternal age show significantly higher stillbirth rates (4.7 times higher) and perinatal (3.8 times) and neonatal mortality (2.6 times) in this cohort compared with the general maternity population in 2002 (table 2). Of the 63 stillbirths, 52 had no congenital anomaly.

Congenital anomalies

A total of 141 major congenital anomalies were identified and confirmed in 109 offspring. The number of offspring with more than one major anomaly was 23 (21.1% of offspring with anomalies). The prevalence of major anomalies in the offspring was 46 per 1000 total births. This compares with 21 per 1000 total births from the European Surveillance of Congenital Anomalies (EUROCAT) data for 2002 (prevalence ratio 2.2, 95% confidence interval 1.8 to 2.6; $P < 0.001$) (table 3).

Discussion

Nearly 15 years on from the St Vincent declaration,¹¹ women with diabetes in England, Wales, and Northern Ireland continue to have high perinatal mortality rates (31.8/1000 births), three times greater than for the general maternity population. Perinatal mortality in European countries and in other UK regional studies of outcomes of pregnancy for women with diabetes range from 27.8 to 48 per 1000 births.^{1-4 12-15}

Near normal metabolic control before and around conception reduces anomaly rates in the pregnancies of women with diabetes,¹⁶⁻¹⁸ and guidance has been issued on the topic.¹⁹ Still, only 37% of women with a recorded HbA_{1c} test achieved good glycaemic control by the end of the first trimester. This does not compare well with the Netherlands, where the corresponding percentage is 75%.¹ We did our study at the same time as the national service framework for diabetes delivery strategy was released,⁵ and the results will be a reference point from which to judge the effectiveness of the framework in tackling this public health concern.

Congenital anomalies

The risk of major congenital anomalies in the offspring of women with diabetes was more than twice that of the general population. Other studies have shown comparable prevalence figures for congenital anomalies, ranging from 41 per 1000 to 97 per 1000, although these studies have been based predominantly on the babies of women with type 1 diabetes.^{1-3 12-15} Comparisons are limited because of differences in inclusion criteria for minor anomalies and early pregnancy outcomes.

In our study, the increased risk of anomalies was predominantly for congenital heart disease (3.4 times higher risk) and anomalies of the nervous system (2.7 times higher risk). In particular, the risk of neural tube defects was three to four times higher than expected. The minimum effective dose of folic acid needed to reduce this risk is not established, but because of the increased risk, women with diabetes should take a higher than usual dose (5 mg) from before conception up to week 12 of pregnancy.^{5 19}

Table 3 Observed (and expected*) anomalies reported in 2400 offspring of women with diabetes

Anomalies	Offspring of women with type 1 diabetes	Offspring of women with type 2 diabetes	Total	Standardised prevalence ratio (95% CI)
One or more major anomalies of any type	81 (37.0)	28 (12.8)	109 (49.8)	2.2 (1.8 to 2.6)
Anomaly system†				
Nervous system:	11 (4.1)	4 (1.5)	15 (5.6)	2.7 (1.5 to 4.4)
Neural tube defects	6 (2.4)	4 (0.9)	10 (2.4)	4.2 (2.0 to 7.8)
Remainder of CNS	5 (1.7)	0 (0.6)	5 (3.0)	1.5 (0.3 to 3.6)
Eye	1 (2.4)	0 (0.9)	1 (1.0)	1.0 (0.1 to 7.0)
Ear	0 (0.7)	0 (0.3)	0 (1.0)	–
Congenital heart disease	33 (8.9)	9 (3.4)	42 (12.3)	3.4 (2.5 to 4.6)
Cleft lip ± palate	0 (1.3)	0 (0.5)	0 (1.8)	–
Cleft palate	2 (0.9)	0 (0.3)	2 (1.2)	1.6 (0.2 to 5.9)
Digestive system	1 (2.6)	2 (1.0)	3 (3.5)	0.8 (0.2 to 2.5)
Internal urogenital system	9 (6.1)	1 (2.3)	10 (8.5)	1.2 (0.6 to 2.2)
External genital system	3 (2.5)	2 (0.9)	5 (3.4)	1.5 (0.5 to 3.4)
Limb, musculoskeletal, and connective tissue	15 (10.2)	4 (3.7)	19 (13.9)	1.4 (0.8 to 2.1)
Other non-chromosomal	6	4	10	–
Chromosomal:	4 (7.2)	2 (4.2)	6 (11.4)	0.5 (0.2 to 1.1)
Trisomy 21	2	0	2	–
Other chromosomal	2	2	4	–

CNS=central nervous system.

*Expected numbers in parentheses based on data from EUROCAT 2002, adjusted for maternal age.

†Multiple anomalies within groups counted only once; total anomalies thus do not add up to 141.

Antenatal diagnosis of some cardiac conditions decreases the risk of neonatal mortality.²⁰ Routine ultrasound scanning for anomalies in the UK has been reported to identify 23% of cardiac defects.²¹ Implementing specialist views of the fetal heart may increase the pick-up rate of cardiac anomalies by up to 75%.²² Our study showed that cardiac lesions were the most frequent anomaly in the offspring of women with diabetes, and 55% were detected antenatally. Current management of pregnant women with diabetes in the UK does not routinely include targeted screening for cardiac defects; this needs to be reviewed.

Type 2 diabetes

In the past decade, type 2 diabetes in pregnancy has emerged as a growing concern.²³ Few population studies have provided perinatal mortality and congenital anomaly rates in women with type 2 diabetes diagnosed before pregnancy. Two of the largest such studies were based on Maori women in New Zealand and Hispanic women in California and may not be generalisable.^{24 25} Other studies have included women in whom the diagnosis of type 2 diabetes was not made until after delivery.^{24 26-28} Reported perinatal mortality in these studies ranges from 6 per 1000 to 313 per 1000 births.^{26 28}

Several studies have reported higher perinatal mortality and congenital anomaly rates in the babies of women with type 2 diabetes than in the babies of women with type 1 diabetes, but they were based on relatively small sample sizes.^{24 27 29-31} Our study shows no evidence of an increased risk. However, even this study was underpowered to detect a significant increase of less than 25% for perinatal mortality and of less than 80% for congenital anomaly, if such increases were present.

Pregnant women with type 2 diabetes were more likely to live in a deprived area or come from an ethnic minority background. Women with type 2 diabetes

What is already known on this topic

Babies born to women with diabetes are known to have increased risks of perinatal mortality and congenital anomalies; most studies have focused on type 1 diabetes

Type 2 diabetes is being diagnosed in an increasing number of women of childbearing age in the UK

What this study adds

The increased risk of anomalies is predominantly accounted for by congenital heart disease and neural tube anomalies

Risks of perinatal mortality and congenital anomalies in the offspring of women with pre-gestational type 2 diabetes are equivalent to those in the offspring of women with type 1 diabetes

often need to change their treatment to insulin before or during pregnancy. The differences in cultural background, first language, lifestyle, and medical care need to be accounted for when considering provision of health services for preconception care and education in this area.

In the past, type 2 diabetes may have been viewed as a less serious condition than type 1 diabetes and may have been subject to less vigilant care.³² In view of the increasing prevalence of type 2 diabetes in young adults, raised awareness of the increased risk of adverse pregnancy outcomes in this group of women is needed.

Conclusion

Women with type 1 diabetes and those with type 2 diabetes both represent high risk groups during pregnancy. We found a threefold increase in perinatal mortality and a twofold increase in the congenital anomaly rate in women with diabetes compared with the general maternity population. Only a minority of women achieved good periconceptional glycaemic control. More work is needed to elucidate how women with either type of diabetes can best be enabled to improve the outcomes of their pregnancy.

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