NICE guidance for neonatal care after diabetes in pregnancy

Diabetes, especially in pregnancy, is an increasing public health concern and a growing challenge for clinicians. Fetal and perinatal morbidity and mortality remain high. Some complications are severe, for example stillbirth and congenital anomalies, while others are transient and unlikely to lead to long-term harm if managed according to published guidelines. On the other hand our concern as clinicians sometimes results in avoidable complications, for example policies of 'routine' admission of a baby to a neonatal unit. Therefore, planning for neonatal management must start in advance of delivery, involve all groups of professionals, and be centred on the needs of the mother and baby.

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Key points

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1. Despite improved maternal care, outcomes are still poor for infants after diabetes in pregnancy.
2. Some complications are related to diabetic control – eg macrosomia, hypoglycaemia.
3. Some complications are iatrogenic – eg preterm delivery, delivery by caesarean section, separation of mother and baby.
4. Best management requires protocols for management of mother and baby, and excellent communication between specialists in the team and with the mother.

Important recent publications (CEMACH Confidential Enquiry reports and NICE guidance) have highlighted the importance of optimal management of diabetes in pregnancy and subsequent best care for the baby[1-4]. Diabetes affects approximately one in 250 pregnant women in the UK, with some regional variation. Type 1 diabetes accounts for about 70% of these pregnancies, while Type 2 diabetes (not traditionally associated with diabetes in women of childbearing age) accounts for 30%[1]. Both types of maternal diabetes are associated with adverse consequences for the fetus and then the neonate, arising from the directly harmful intrauterine metabolic environment, or the obstetric interventions required when maternal control is poor, or from inappropriate 'routine' practices. The best possible diabetic control minimises risks to the mother and the fetus, and reduces the risk of postnatal complications, described below.

Care of the healthy infant after pregnancy complicated by diabetes

For many women, especially those who access prenatal counselling and specialist care for management of diabetes in pregnancy, fetal and neonatal complications related to diabetes in pregnancy are unlikely. It is very important to recognise that a baby at very low risk of complications should be managed according to normal standards for the healthy newborn baby – mother and baby should not be separated and breast feeding should be encouraged[4,5]. However, it is necessary to be aware of the possibility of complications which may not be immediately obvious at birth.

Neonatal complications

Unfortunately, recent data suggest that insufficient progress has been made in the reduction of perinatal mortality and morbidity associated with diabetes in pregnancy[1,2,6]. Some of the complications are secondary complications of intrauterine or intrapartum hypoxia-ischaemia or the abnormal metabolic environment that the fetus of a diabetic mother may be exposed to. Some arise from the effects of being born preterm or by caesarean section, and some neonatal problems are iatrogenic (arising from clinical interventions that are not always required) (**TABLES 1 and 2**).

Perinatal mortality

The stillbirth rate for women with types 1 and 2 diabetes in the UK in 2002-2003 was 4.7 times more common than the national rate (26.8/1000 births compared to a national rate of 5.7/1000). Similar rates are reported from Europe[1,6]. If born alive, babies of mothers with diabetes are 2.6 times more likely than expected to die during the neonatal period (9.3/1000 live births compared to a national rate of 3.6/1000)[1]. The most common causes of neonatal death are congenital abnormality and intrapartum complications[2]. Overall,

- Perinatal mortality
- Complications of preterm delivery
- Complications of caesarean section
- Hypoxia-ischaemia
- Macrosomia, obstructed labour, birth injury
- Polycythaemia/jaundice
- Congenital anomalies
- Intrauterine growth restriction
- Hypoketonaemic hypoglycaemia
- Hypocalcaemia, hypomagnesaemia
- Hypertrophic cardiomyopathy
- Iatrogenic – eg separation of mother and baby, impaired breast feeding

TABLE 1 Possible neonatal complications after diabetes in pregnancy.

	IDM	UK	Ratio
Neonatal death	9.3/1,000	3.6/1,000	2.6
Preterm delivery	37%	7.3%	5
Congenital anomaly	5.5%	2.1%	2.6
Birthweight >90th centile	52%	10%	5.2
Shoulder dystocia	7.9%	3%	2.6
Erbs palsy	4.5/1,000	0.42/1,000	11
Apgar <7 at 5 mins	2.6%	0.76%	3.4
Admission NNU	56%	10%	5.6
Term admission SC	33%	10%	3.3

NNU – neonatal unit, SC – special care, IDM – infant of diabetic mother

TABLE 2 Neonatal outcomes (CEMACH 2005)[1].

the perinatal mortality rate with diabetes in pregnancy in 2002-2003 was 31.8/1000 in UK and 27.8/1000 in The Netherlands, compared to a national UK rate without diabetes of 8.5/1000 (a rate ratio of 3.8)[1,6].

Preterm delivery

In the UK in 2002-2003, women with diabetes were 4.8 times more likely than expected to have a preterm baby (<37 weeks' gestation) (35.8% compared to a rate of 7.4% in the general population)[1]. A study from The Netherlands has provided similar data[6]. There must always be a balance between continuing a pregnancy until term and reducing the time both fetus and mother are exposed to a harmful environment, if diabetes is not well controlled. However, for women in the 2002-2003 cohort, 19% had preterm delivery that was not spontaneous or explained by maternal or fetal compromise and thus could have been avoided[1].

If preterm delivery is planned, this must be at a unit that can provide the appropriate level of neonatal care within a perinatal network. Maternal steroids must be given, according to standard practice. In the cohort of women with diabetes in pregnancy in 2002-2003, 70% of women who delivered live babies between 24 and 34 weeks' gestation received prophylactic antenatal steroids[1].

Once born, there is no evidence that the usual complications of prematurity are more severe than for a gestation age-matched baby whose mother does not have diabetes. Preterm babies of diabetic mothers should be managed according to standard protocols. In particular mothers should be encouraged to express breast milk, and arrangements to facilitate this must be made. The additional problems specific to the baby of a diabetic mother that may occur and need additional management are shown below.

Effects of delivery by caesarean section

In the 2002-2003 UK cohort, the caesarean section rate was 42.7%, and in The Netherlands the rate was 44.3%[1,6]. Nine per cent of UK caesarean sections were not explained by maternal or fetal compromise and thus could have been avoided, and 4% were 'routine for diabetes' or 'maternal request'[1]. As stated above, a number of these 'routine' caesarean sections were at preterm gestation.

While the benefit to the baby of caesarean section is protection from hypoxic-ischaemic brain injury, the potential adverse effects on the baby of unnecessary caesarean section (eg delayed and disrupted breast feeding and respiratory morbidity) must be considered[7,8]. These complications, in turn, frequently result in avoidable admission to a neonatal unit and separation of mother and baby.

Hypoxia-ischaemia, polycythaemia

In the enquiry into diabetic pregnancies in 2002-2003, 10% of perinatal deaths were related to intrapartum causes[2]. The mechanisms of intrauterine loss and neonatal complications secondary to hypoxia-ischaemia are poorly understood. In some cases, macrosomia and obstructed labour may contribute to intrapartum hypoxia-ischaemia. Delivery of babies of diabetic mothers must occur at units where advanced neonatal life support is available, and arrangements must be made to transfer a baby with hypoxic-ischaemic encephalopathy for continuing care on the appropriate level neonatal unit. If total body cooling becomes an established treatment for hypoxic-ischaemic encephalopathy, time is of the essence in commencement of this treatment at a specialist centre[9].

Increased fetal red cell production is known to occur in many fetuses when pregnancy is complicated by diabetes[10]. The resulting neonatal polycythaemia may then cause excessive neonatal jaundice (as the red cell burden is dissolved) and occasionally hyperviscosity syndrome. Renal vein thrombosis or thrombosis in other vessels is rare, but occurs more frequently than in babies whose mothers do not have diabetes. Polycythaemia associated with clinical signs must be treated with partial exchange transfusion.

Congenital anomalies

It has long been recognised that there is a higher incidence of congenital anomalies after diabetes in pregnancy, than in the general population[11]. Most recent UK data on diabetes in pregnancy demonstrate that 4% of fetuses had one or more major congenital anomaly (twice that reported in the general population)[1]. The reported incidence was even higher in The Netherlands[6]. The most common anomalies are congenital heart malformations, and anomalies of limb, musculoskeletal system or connective tissue. Neural tube defects, although numerically rare, are 3.4 times more common than in the general population[1].

The most important aspects of management are adequate counselling of parents, involving the specialist team who will care for the baby postnatally, and

ensuring delivery is at an appropriate centre to enable early access to specialist care, depending on the nature of the anomaly. Routine postnatal echocardiography to screen for congenital heart anomalies is not indicated, unless there has been an antenatally diagnosed lesion or the baby presents with clinical signs of congenital heart disease[4].

Macrosomia, obstructed labour, birth injury

Macrosomia and organomegaly attributed to fetal hyperinsulinaemia are well known characteristics of many diabetic pregnancies, but evidence is inconsistent regarding the potential impact of improved diabetic control[6,12]. Rate of macrosomia (birthweight above 90th centile) was 52% in the recent UK cohort[1] (**FIGURE 1**).

The clinical significance of macrosomia is the risk of the complications of delivery of a large infant, such as shoulder dystocia (twice the rate as in the general population), obstructed labour, perinatal hypoxia-ischaemia, brachial plexus injury (10 times the rate as in the general population) and fractured clavicle or humerus[1].

Parents and health professionals must be prepared for postnatal 'catch down' in growth of macrosomic babies, especially when breast fed. This is a normal and healthy adaptation, and to over feed the baby and have it remain overweight has long-term health consequences, eg later risk of cardiovascular disease and diabetes[10]. This is a further reason to promote and support breast feeding.

Intrauterine growth restriction

Placental insufficiency, often associated with severe diabetic vasculopathy or frequent maternal hypoglycaemia, can impair fetal growth. The small for gestational age infant of the diabetic mother appears to be at even greater risk of adverse outcome, especially neuro-developmental sequelae[13]. Delivery must be planned at an appropriate unit if specialist neonatal care is likely to be required.

Impaired postnatal metabolic adaptation

After maternal diabetes, the neonate is at risk of transient hyperinsulinism which in turn causes a high rate of glucose uptake and conversion to fat, reduced glucose production, and reduced lipolysis and thus reduced production of ketone bodies (which are alternative fuels to glucose)[10,14] (**TABLE 3**). Although it has been suggested that neonatal hypoglycaemia has neurodevelopmental consequences, no study has been able to exclude other potentially confounding complications of maternal diabetes which may also influence outcome[10,14]. Clinically significant hypoglycaemia, associated with physical signs is in fact rare. However, it is important to detect at an early stage the few cases when hypoglycaemia becomes clinically significant and then institute appropriate management. Management is covered in detail in many standard texts – care must be individualised for each baby, against a background of careful clinical evaluation[3,4,10,14-17] (**TABLE 4**).

Clearly, babies who are preterm or unwell and admitted to neonatal units will undergo blood glucose monitoring as part of their clinical care. However, unless the baby has clinical complications sufficiently severe to require admission to a neonatal unit, mother and baby must remain together. Those caring for the baby must assure themselves at regular intervals that the baby has normal feeding behaviour and no abnormal neurological signs, and must document their findings. Unless there are risk factors for other complications (eg infection) and the baby appears well, it is not necessary to monitor vital signs (temperature, pulse, respiration rate) or to screen for other potential complications eg polycythaemia. If at any stage there are abnormal clinical signs, blood glucose level must be measured and an urgent

FIGURE 1 Macrosomia is a feature of diabetic pregnancies.
Photo credit: Pearson ER, Boj SF, Steele AM, Barrett T, Stals K, et al. Macrosomia and hyperinsulinaemic hypoglycaemia in patients with heterozygous mutations in the HNF4A Gene. PLoS Med 2007; 4(4): e118.

- Maternal hyperglycaemia and amino acids
- Excess transport across placenta
- Fetal hyperinsulinism
- Neonatal hyperinsulinism
- Hypoketonaemic hypoglycaemia

TABLE 3 Causes of impaired neonatal metabolic adaptation.

- Maternal control, especially prior to delivery, influences risk
- Accurate method of blood glucose monitoring required
- Formula supplementation is likely to suppress normal metabolic adaptation
- Formula feeding may increase risk of later obesity and metabolic disturbance
- Minimise separation and its impact on breast feeding

TABLE 4 Principles of management of neonatal hypoglycaemia.

paediatric review arranged.

It is generally accepted that infants of diabetic mothers should have regular blood glucose monitoring[4]. However, given that clinically significant hyperinsulinism and hypoglycaemia appears rare in the UK, the team caring for a mother and baby may choose to take into account good diabetic control in pregnancy and clinical normality of the baby, and elect not to measure blood glucose levels. This could not be criticised provided there is documentation of this rationale, of regular assessments of clinical condition and feeding, and the triggers for commencing blood glucose monitoring.

Blood glucose monitoring should not be commenced before three to four hours of age. To commence sooner than this is not informative, as babies experience a physiological transitional fall in blood glucose level in the first hours after birth. Blood glucose monitoring should be pre-feed in order to detect the lowest blood glucose level. In a baby with no clinical signs, a post-feed glucose level is not helpful and exposes the baby to excessive heel stabs.

Blood glucose monitoring must be by an accurate, laboratory-based method. No near patient testing device has been demonstrated to be sufficiently accurate to diagnose or exclude neonatal hypoglycaemia. Some neonatal units have an accurate and quality assured analyser sited in the unit laboratory, which is the recommended standard[1-4,14,15,18]. However recent data indicate that only around 25% babies had blood glucose monitoring using accurate methods[1].

There is no doubt that a low blood glucose level associated with clinical signs must be treated. Clinical signs suggestive of (but not specific to) hypoglycaemia are – abnormal tone, abnormal level of consciousness, poor oral feeding, and fits, which may be atypical eg presenting as apnoea. Management of a low blood glucose level associated with abnormal clinical signs is a medical emergency and will necessitate full clinical evaluation and often transfer to a neonatal unit. If clinical signs are not severe (eg alert baby but poor suck), it is reasonable to assess the effect of tube feeds at an appropriate interval. However, if blood glucose levels do not increase with tube feeds or the baby has serious clinical signs (eg reduced level of consciousness or fits) intravenous glucose must be given without delay[19].

In the absence of abnormal clinical signs, recommendations for blood glucose thresholds at which to intervene must be pragmatic, and must balance the risks of developing clinically significant hypoglycaemia against the risks of disrupting breast feeding and separating mother and baby. NICE guidance advises that, in the absence of clinical signs, two consecutive blood glucose levels below 2.0mmol/L require intervention to aim to raise the blood glucose level[4].

Breast feeding is the method of choice for all babies (barring rare exceptions eg maternal HIV infection). Having diabetes is not a contraindication to breast feeding. However in the UK cohort, only 53% of mothers with diabetes intended to breast feed, and at 28 days only 27% of term babies were breast fed[1]. Mothers should be encouraged antenatally to consider breast feeding their baby and should receive sufficient information to make their choice. Immediately after delivery a healthy baby should be placed skin-to-skin with mother and an early breast feed offered, with assistance to ensure the baby achieves an effective latch. Breast feeds should be offered 3-4 hourly (or more frequently if the baby demands), again with support if necessary.

Formula supplements to breast feeds are only required if there are clinical indications, including the requirement to intervene for hypoglycaemia. Formula supplements result in the baby feeding less from the breast, and thus reduced breast milk supply, and suppress normal postnatal metabolic adaptation[14]. Finally, the long term metabolic risks of over feeding and obesity in infancy must be guarded against. Therefore, if formula supplementation is required, this must be at a volume required and no more. If a mother and baby are separated, or if the baby requires formula supplements to breast feeds, the mother should be encouraged to express breast milk, which allows lactation to be sustained and provides breast milk which can be given to the baby.

If hyperinsulinism does occur, it will present in the first 1-2 postnatal days and will be transient, lasting a maximum of a few days. Therefore, if a baby is clinically stable and has shown no evidence of clinically significant hypoglycaemia, blood glucose monitoring may be discontinued when glucose levels are above 2.0mmol/L and the baby may be discharged to community care from 24 hours of age if all else is well[4].

Hypocalcaemia, hypomagnesaemia

Transient neonatal hypocalcaemia has been reported following diabetes in pregnancy and both its incidence and severity appear to be related to the degree of maternal diabetes control[10]. It is usually associated with hyperphosphataemia and occasionally with hypomagnesaemia. As this complication is rarely of clinical significance, routine monitoring is not indicated. Hypocalcaemia and hypomagnaeaemia associated with clinical signs should be treated with appropriate supplements.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy characterised by hypertrophied septal muscle which obstructs the left ventricular outflow tract may be sufficiently severe to cause fetal or neonatal death[10] (**FIGURE 2**). In less severe cases, the presentation is

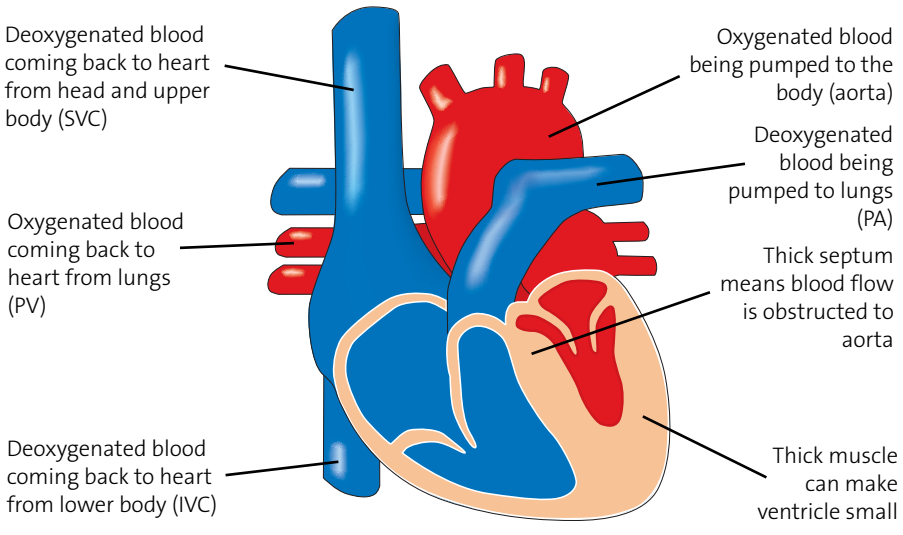

FIGURE 2 A diagram of a heart demonstrating hypertrophic cardiomyopathy.

usually within the first weeks of postnatal life with cardiorespiratory distress and congestive heart failure. The majority of these infants need supportive care only, as resolution of the signs can be expected in 2-4 weeks. The septal hypertrophy regresses within 2-12 months. Routine postnatal echocardio-graphy is not required unless there are clinical signs[4].

Iatrogenic complications

As discussed above, the timing and method of delivery often impacts upon neonatal morbidity. However, even if there are no significant maternal or fetal complications and the pregnancy goes to term or near term, the evidence is that the baby is still exposed to potential iatrogenic harm (**TABLE 5**). The CEMACH enquiries demonstrated frequent failings in medical and midwifery care:

- 'routine' admission of babies to neonatal units
- 'routine' supplementation or replacement of breast feeds with formula
- delayed skin-to-skin and first feed, poor management of temperature control
- blood glucose tested and acted upon too soon after delivery[2,3].

In addition to the harmful effects for mother and baby, these represent an avoidable use of neonatal unit resource.

Conclusion – avoiding harm

The findings from many published studies and now the CEMACH enquiries have reinforced the recommendations for good practice which are associated with reduction in postnatal complications and iatrogenic harm[1-4,6]. All hospitals must have written protocols for the prevention and management of potential neonatal complications, including hypoglycaemia.

- 16% preterm deliveries – no clear indication
- 30% preterm deliveries had no maternal steroids
- 5% babies delivered with no HD/IC facility
- 25% admitted term babies – 'routine'
- 9% received formula – 'routine'

CEMACH 2005[1], 2007[2]

TABLE 5 Avoidable adverse outcomes for baby.

When neonatal complications are expected, the baby must be delivered in a unit where the appropriate expertise is present, the minimum standard for all diabetic pregnancies being a hospital where advanced neonatal life support skills are immediately available. However, of equal importance is to avoid iatrogenic harm by avoiding unnecessary preterm delivery or caesarean section and unnecessary separation of baby and mother. This requires high standards of communication between professionals and with the women they care for.

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