



Insulin Dependent Diabetes Trust

Pregnancy and Diabetes

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Most women with diabetes are aware that pregnancy means that they face greater risks to their own health and that of their baby than women without diabetes.

For women considering having a baby, it is important to have information and advice before conception and throughout pregnancy.

It is also important to know that breastfeeding and weaning affect blood glucose control.



Facts

A study published in 2002 in Finland [Diabetic Medicine 2002, Vol

19] looked at pregnancy from 22 weeks to one year after birth. The results showed:

- The rate of congenital abnormalities in babies born to women with diabetes has not changed in recent years.
- The perinatal mortality remains 3-5 times higher in women with diabetes than in non-diabetic women.
- The proportion of perinatal deaths caused by congenital abnormalities has reduced but the post-natal mortality has significantly increased.
- Diabetic mothers of malformed babies were significantly younger than mothers of babies that were not malformed.
- Nearly two thirds of the malformed babies were boys.

The study points out that the reduction in perinatal deaths and increase in post-natal deaths could be due to better care during pregnancy. But it is also worth noting that the mortality rate in the general population has also reduced markedly. In England in 1960 it was 32.5 per 1000 total births compared with 7.6 per 1000 births in 1992. [A perinatal death is usually defined as death of the foetus after 28 weeks of pregnancy and the first week of the baby's life.]

A study published in April 2004 carried out at the University Medical Centre Utrecht [www.bmj.com] followed 323 women with Type 1 diabetes who became pregnant during 1999 and 2000. The study showed that 84% of the pregnancies were planned suggesting that blood sugar control was good in early pregnancy and most women were taking folic acid. Yet despite this:

- More than 12% of the pregnancies were complicated by pre-eclampsia - 12 times higher than the general population.
- 32.2% of babies were born prematurely [before 37 weeks] - a fourfold increase in risk compared to non-diabetic women.
- There is a high risk of babies being born with dangerously low blood glucose levels, hypoglycaemia.
- 44.3% had Caesarean births - again a fourfold increased risk.
- Congenital abnormalities, such as heart problems occurred in 29

babies - 3 times the number for the general population. The researchers concluded that even near perfect control of blood glucose levels during pregnancy was not sufficient to guarantee protection of mother and child.



Latest NICE Guidelines

Pregnancy and diabetes

The latest National Institute for Health and Clinical Excellence (NICE) guidelines on pregnancy and diabetes were issued in May 2008. They recommend that:

- women with diabetes should be able to access specialist services before they become pregnant.
- They should aim for a fasting blood glucose of 3.9 to 5.9mmol/l and one hour post-prandial [after meals] blood glucose below 7.8mmol/l if planning to become pregnant and during pregnancy.
- Women should be directed to take folic acid supplements and given lifestyle advice.
- They should be told of the importance of maintaining vitamin D levels during pregnancy and while breast feeding and if required, they should be offered Vitamin D supplements.
- Health professionals should advise on good glycaemic control in reducing the risk of miscarriage, malformation at birth, still birth and neonatal death.
- GPs must tell women who are pregnant and those planning to conceive to avoid alcohol because it can increase the risk of miscarriage in the first trimester.
- Women with gestational diabetes should be offered advice on diet and exercise and offered a fasting plasma glucose test at the 6-week postnatal check and yearly after that.



Pre-conception

It has been known for some years that good diabetic control at the time of conception improves the chances of having a healthy baby. Entering the pregnancy with good control increases the chances of a healthy baby because important organs of the foetus develop during the early part of pregnancy - the brain, the spine, the heart, the kidneys and the gastrointestinal system. Malformations associated with diabetes are spina bifida, where the spine does not completely close and heart defects. As these malformations are formed during early pregnancy, getting into better control later in the pregnancy does not change what has already developed. However, it is important to remember that just because a woman does not have good control she is bound to have a baby that is affected.

For these reasons, a planned pregnancy with good blood glucose control at the time of conception is the ideal situation although it is estimated that as many as two thirds of pregnancies are unplanned. A planned pregnancy also means that folic acid supplements, which reduce the risk of spina bifida and other defects, can also be taken prior to conception. Many diabetes clinics now offer 'pre-conception counselling' for couples intending to have a baby to try to ensure that the mother's blood glucose control is good at conception and from the outset of the pregnancy.

Just a note: Also worth checking at this stage is the safety of the insulin you are using and any other drugs. None of the analogues have been tested in pregnant women or those planning pregnancy so any risks to the foetus and/or mother are unknown. Commonly prescribed for people with diabetes are ACE-inhibitors for the treatment of blood pressure and/or to slow down the progression of kidney disease and also statins to reduce cholesterol levels. Both these classes of drugs are potentially toxic for the foetus.

But do women attend pre-conception counselling?

Researchers in Hull [ref1] who carried out a study looking into the use of Humalog during pregnancy were struck by the large number of women in this study who did not have pre-conception counselling.

Despite the fact that this was freely available to them – only 40% took it up.

So they carried out a questionnaire study in 69 women between the ages of 16 and 45 to survey their attitudes and knowledge of maternal diabetes and pregnancy. 18 of the women already had children and the rest didn't. The results were surprising but according to the researchers are similar to other studies:

- In both women with and without children, a high proportion of women [85%] knew that their diabetes could affect the health of the baby and that good control was important at the time of the conception.
- Of the 18 with children only 44%, less than half, had attended pre-conception counselling before their last pregnancy.
- Only 52% of those without children and 28% of those with children reported the intention to do so before a future pregnancy.

So although the knowledge about the need for pre-conception counselling was there, this knowledge is not acted upon. What is more, the women that had already had one pregnancy were even less likely to seek counselling before a future pregnancy! The researchers point out that teaching and knowledge do not necessarily change behaviour and they suggest that a novel approach is needed if pregnancy outcomes are to be improved and that this should continue throughout the reproductive years.

Just a comment...

It is a shame that the questionnaire did not ask why women don't attend pre-conception counselling. It is well recognised that pregnant women with diabetes go to great lengths to maintain very tight blood sugars to safeguard the health of the baby and indeed, their own health, so it is surprising that so few women attend. Perhaps the term 'Pre-conception counselling' is not one that appeals to people contemplating having a baby, especially young people! The word counselling alone can be off-putting for some people. Straight forward 'Family Planning' may be more appealing but a little imagination would

Pregnancy

Blood glucose control throughout pregnancy

Blood sugar control is important throughout pregnancy but for different reasons. In the early stages of pregnancy it is important for the healthy development of the foetus and in the later stages, it is important to avoid hyperglycaemia because of the impact on the baby's metabolism.

Excess glucose in the mother's circulation easily passes through the placenta to the baby and it is as if it is eating sweets all the time. This stimulates insulin production in the baby, insulin is a potent growth hormone and so fat is deposited. This can result in a large baby which can lead to complications at delivery because the baby will not easily fit through the birth canal. After delivery the baby still produces large amounts of insulin which can result in the new born baby being hypoglycaemic. The hypoglycaemia can be dealt with by the paediatrician.

The first trimester – the first 3 months

Low blood sugars are more common during the first 3 months of pregnancy because the baby begins to feed off the mother's glucose stores. In addition to this, the hormones are working hard to create the placenta and this can make it hard to control blood sugars. So it is important to blood test frequently and be prepared for unexpected hypos. Sometimes during this period the symptoms of hypos may change and you may not always recognise them, so it is advisable to warn friends and work colleagues about the signs of hypos. If you don't already have glucagon for emergencies, then it may be a good idea to discuss this with your doctor. Glucagon is an emergency hormone that is injected if you have a severe hypo and are unconscious so

cannot eat or drink. It works by making the liver release its own stores of glucose.

Morning sickness is common in 70% of pregnant women. It is worse on an empty stomach and some women find that eating a cracker or something similar may help. It may also help to make sure that you have a bedtime snack with protein and carbohydrate. Sometimes eating smaller and more frequent meals helps. If morning sickness is a real problem, you should discuss this with your dietitian. If it is so severe that you are vomiting up to 10 times a day, then you should call your doctor because there is a risk of ketoacidosis [very high blood sugars that are out of control].

The doses of insulin you need may change frequently because of the body's hormone activity during this time. It may also be necessary to change your insulin regime – your meal times and injection times.

The second and third trimesters [4 to 9 months]

During this time insulin requirements usually increase and could be as high as two or three times your normal daily amount. This is because the placenta produces a hormone that makes it more difficult for the insulin to work. So frequent testing and dose adjustments when necessary are essential. Once the baby is born, insulin requirements quickly drop back to normal.

During this time the doctors will continue to monitor your blood glucose levels, blood pressure and kidney function. Some women with and without diabetes develop high blood pressure and oedema [fluid retention causing swelling] during the latter part of their pregnancy. If this is left untreated it can lead to pre-eclampsia which puts both mother and baby at risk.

Labour

Many women with diabetes go into natural labour and delivery is normal but this depends largely on the baby's size and position. Women with diabetes tend to have bigger babies and so if the baby is large it may have problems moving safely through the birth canal.

This is one of the reasons the healthcare team monitor the health and size of the baby very closely. If the baby is large then labour may be induced.

The decision to induce labour is usually taken after 36 weeks and this will depend on the baby's size, the maturity of its lungs, the health of the placenta and the mother's health.

If the baby is too large or the health of mother and baby is at risk then a Caesarian section will be carried out. This is much more common in women with diabetes than in women without diabetes.

Caesarian Section

Women with diabetes are more likely to give birth by Caesarean section as their babies tend to be larger, labour tends not to progress as smoothly and/or if the mother's safety is at risk. If the mother to be has diabetes complications this can make vaginal delivery of the baby more dangerous for both mother and baby. However, giving birth by Caesarean section has disadvantages:

- Diabetes increases the chances of infection and can slow down wound healing so making surgery such as a Caesarian section more risky.
- Caesarean section means a longer stay in hospital, greater chance of transfusions and a slower recovery.

If a woman has had one Caesarean section does it mean that this will happen with the birth of subsequent children?

A study published in The Journal of Reproductive Medicine [Dec 2000] looking at 127 women most of whom had already given birth by Caesarean showed that only 43.7% of diabetic women that attempted vaginal birth after a Caesarean, succeeded but in women without diabetes 60 – 80% of them had successful vaginal births after a

Caesarean. The authors of the study called for more research because they felt unable to conclude that vaginal birth after a Caesarean was safe for women with diabetes.

New techniques for Caesarean sections

Research carried out in Austria, published in the Journal Obstetrics and Gynaecology [January 2003], describes a new technique for Caesarean sections which is less painful and far quicker than past methods, taking about 20 minutes in all. The new method reduces blood loss in the mother by half so cutting the length of the procedure and allowing the mother to recover more quickly.

The new method means that doctors use a sharp knife to cut the skin but then blunt instruments to gently pull the uterine wall apart and deliver the baby. This compares with sharp dissection used by some doctors. The women need fewer stitches because only three layers need to be stitched compared to between four and seven in other methods.

Professor James Walker of the Royal College of Obstetricians and Gynaecologists reported that many aspects of this technique are already in use in Britain as this is 'good practice'. Perhaps this is a question that mothers-to-be should raise during pregnancy.

In April 2004 the National Institute for Clinical Excellence [NICE] introduced guidelines on Caesarian Section and there is a section that provides information for pregnant women, their partners and the public. This can be obtained as a booklet and can be ordered from the NHS Response Line: tel 0870 1555 455 quoting reference number N0479 or it can be viewed by visiting the NICE website www.nice.org.uk/CG013NICEguideline

Breast Feeding

A great deal is published about pregnancy and women with diabetes but what about after the birth? It is difficult to find research that deals with the effects of breast feeding on diabetic mums and the control of their diabetes.

There is no reason why women with diabetes should not breast feed like any other mum. Breast milk production uses a lot of glucose/ carbohydrate from the mother's supply so it is important to avoid hypoglycaemia by lowering insulin doses as necessary. According to the Nutritional Subcommittee of Diabetes UK, [Diab Med 20.786-807] the high energy needs of lactation mean that a mother is likely to require 40-50g carbohydrate per day compared with pre-pregnancy amounts. Extra carbohydrate may be required before going to bed while the baby is still having night feeds. However, once breastfeeding stops, insulin doses and carbohydrate intake will need to be changed. Although only small, a published study [Pract Diab Int October 2003, Vol.20 No.8] showed:

- in both breastfeeding and non-breastfeeding mothers with Type 1 diabetes glucose levels were lower during the first week after delivery.
- Insulin requirements remained lower than before pregnancy throughout the 2 months after the baby is born, whether the mothers were breastfeeding or not.
- Hypoglycaemia does not occur more frequently during or immediately after breastfeeding.

Weaning

There seems to be even less information on how to deal with weaning and advice is usually given on the basis of common sense. If you have been doing a lot of regular exercise and then you stop your blood sugars would go up unless you either ate less or increased insulin doses. The same applies when milk production ceases when the child is weaned.

Although there is little research on this, the general advice for diabetic

mums is that weaning should be done gradually so that adjustments in diet and insulin can be slow and smooth. Natural weaning where the child outgrows his/her need for breast feeding, is the easiest to allow the mother's body to adjust. But if there is an active decision to wean the baby, then reducing breastfeeds by no more than one feed per week seems to be the general advice. This enables blood glucose control to be more easily managed.

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Report - Diabetes in Pregnancy: Caring for baby after birth [2007]

Do babies of diabetic mothers need to be placed in special care units? This is an issue that has been raised with IDDT as pregnant women with diabetes have been advised that their newborn babies will be removed from them and placed in the special baby care unit. Some women are told that this is a necessary and normal procedure – even in hospitals with a 'good reputation'. While this could be necessary on health grounds, many diabetic mothers are being separated from their babies for no other reason than hospital convenience or 'hospital policy'.

The findings of a national inquiry, the Confidential Enquiry into Maternal and Child Health [CEMACH] produced in a report, Diabetes in Pregnancy: Caring for baby after birth [2007], stated that in over half of mothers with Type 1 and Type 2 diabetes their newborn babies are automatically moved to a special care baby unit when there was no specific medical indication for admission and in other cases because babies were not being kept warm enough. This leads to unnecessary separation of babies from their parents. The report goes on to confirm that there are many benefits of early interaction between mother and baby and hospitals should have policies to enable this to happen.

The author of the report stated: *"Babies of mothers with diabetes have more complications and do need careful monitoring, nevertheless in*

the absence of specific risks or complications, every effort should be made to ensure that these babies can be kept with their mothers safely in order for bonding, temperature control and breast feeding to take place.”

The report also shows that there were a number of barriers to breastfeeding and these were:

- A quarter of babies did not have early feeding on the labour ward.
- Instant formula was given as first feed to two thirds of babies.
- Maternal choice not to breastfeed was the main reason for instant formula feeding on the postnatal ward.
- The first blood glucose test was often performed too early to be informative, with inaccurate methods of testing used and insufficient documentation of management.
- The report recommends that:
- Mothers with diabetes to receive advice about the benefits of breastfeeding for their child during the antenatal period.
- Babies to be with their mothers immediately after birth, provided there are no postnatal complications. Early mother-baby contact helps to establish breastfeeding and to regulate the temperature in babies.
- Encouragement of breastfeeding within an hour of birth, but all mothers should be supported in the feeding method of their choice.
- Better guidelines and training for healthcare professionals in the management of babies of mothers with diabetes.

IDDT advice to pregnant women with diabetes: make sure that you know the hospital system before you are due to have your baby and make it clear that you don't want to be separated from your newborn baby unless there are medical grounds for doing so.

Insulin and pregnancy

Pregnant women or those considering pregnancy are always concerned about any medications they take at this time. Clearly women with diabetes have to take insulin but still need to know about any safety issues for both themselves and the unborn baby. For the newer insulin analogues it is important to know that the information about their safety is limited as trials have not been carried out in sufficient numbers of pregnant women. Here is some information that may be helpful.

The use of insulin during pregnancy

Introduction

Insulin was discovered and first used to treat diabetes in the 1920s. The first insulin used was beef insulin [extracted from the pancreases of cattle] and in the 1970s highly purified pork insulin [extracted from the pancreases of pigs] first came on the market. So beef and pork insulins, now both highly purified, have a long history of safety.

Synthetic genetically modified human insulin [made from bacteria by DNA technology] was introduced in 1982 and widely used as first line treatment by the end of that decade. From 1998 insulin analogues were introduced and they are made by a further genetic modification of human insulin. Scientific evidence has shown that for the majority of people, insulin analogues are not superior to human insulins.

The vast majority of people use human insulin without any difficulties but a significant number of people experience adverse effects when using the human and analogue insulins and need natural animal insulin.

Some of the newer insulins have not been tested in pregnant women and therefore warnings are issued in the Specific Product Characteristics [SPC] information.

Below is a list of the statements from the manufacturers about the use of various insulins during pregnancy.

It is wise to interpret the expressions used by drug companies:

- 'Limited clinical experience in pregnancy' – means that no or few clinical trials have taken place.
- 'No clinical data on exposed pregnancies are available' – no clinical trials have taken place.
- 'No clinical experience during pregnancy' – no clinical trials have taken place.
- 'Information on large numbers of exposed pregnancies do not indicate any adverse effect on pregnancy' – this does not state that trials have been carried out and implies that the information is observation.
- 'Data on a large number of exposed pregnancies do not indicate any adverse effect' – does not mean that it has been proved to be safe.

Animal insulins

Hypurin Porcine Neutral and Hypurin Isophane insulins

A decreased requirement for insulin may be observed during the early stages of pregnancy. However, in the second and third trimesters, insulin requirements may increase. Insulin requirements should therefore be assessed frequently by an experienced physician. Diabetic patients who are breast-feeding may require adjustments to their insulin dose.

Note: no warnings against use in pregnancy.

Human insulins

Human Actrapid and Human Insulatard

There are no restrictions on treatment of diabetes with insulin during pregnancy, as insulin does not pass the placental barrier.

Humulin insulins

There is no mention of any restrictions on use in pregnancy.

Human Insuman insulins

For insulin human, no clinical data on exposed pregnancies are available. Insulin does not cross the placental barrier. Caution should be exercised when prescribing to pregnant women.

Analogue insulins

Humalog and Humalog Mix 25

Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin lispro [Humalog] on pregnancy or on the health of the foetus/newborn.

NovoRapid

NovoRapid (insulin aspart) can be used in pregnancy. Data from two randomised controlled clinical trials (322 and 27 exposed pregnancies) do not indicate any adverse effect of insulin aspart on pregnancy or on the health of the foetus/newborn when compared to human insulin.

NovoMix 30

There is limited clinical experience with NovoMix 30 in pregnancy. Animal reproduction studies have not revealed any differences between insulin aspart and human insulin regarding embryotoxicity or teratogenicity.

Apidra

There are no adequate data on the use of insulin glulisine [Apidra] in pregnant women.

Animal reproduction studies have not revealed any differences between insulin glulisine and human insulin regarding pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women. Careful monitoring of glucose control is essential.

Lantus

For insulin glargine no clinical data on exposed pregnancies from controlled clinical trials are available. A limited number of exposed pregnancies from Post Marketing Surveillance indicate no adverse effects of insulin glargine on pregnancy or on the health of the foetus

and newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct harmful effects with respect to pregnancy, embryonal /foetal development, parturition or postnatal development.

The available clinical data is insufficient to exclude a risk. The use of Lantus may be considered in pregnancy, if necessary.

Levemir

There is no clinical experience with insulin detemir [Levemir] during pregnancy. Animal reproduction studies have not revealed any differences between insulin detemir and human insulin regarding embryotoxicity and teratogenicity.

Caution should be exercised when prescribing to pregnant women.

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Research

Very tight versus tight control for diabetes in pregnancy

Pregnancies complicated by pre-existing insulin dependent diabetes are high risk for a number of poor pregnancy and neonatal outcomes. The objective of this review was to assess the effects of very tight glycaemic control compared with tight control in women with Type 1 diabetes.

Main results: Two trials involving 182 women were involved. The two trials were difficult to compare. Maternal hypoglycaemia was more common among women whose diabetic control was very tight compared to tight control based on one trial. There was no difference detected in perinatal outcome between the groups.

Reviewers' conclusions: There appears to be no clear evidence of benefit from very tight glycaemic control for pregnant diabetic women. Since very strict control may have a substantial impact on lifestyle, this suggests caution in advising such a tight degree of control.

Diabetes Care in Pregnancy

3.12.02 reported in the British Medical Journal

Researchers in Norwich studied 158 pregnancies in women with Type 1 diabetes between 1991 and 2000. The women were divided into two groups – one that had fair control and the other that had poor control of their blood glucose levels. The researchers defined adverse pregnancy outcome as spontaneous abortion, congenital malformation, still birth or infant death. They found that adverse outcomes were fourfold higher in the poor control group compared to the fair control group. The poor control group had a ninefold increase in congenital malformation that was potentially life threatening or linked to long-term disability.

The authors of the study recommend that diabetic women and their carers need to be advised of the risks and encouraged to optimise glycaemic control before and during pregnancy.

For a leaflet on Gestational Diabetes contact:
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