Gestational diabetes: Prophet and predictor

Jackie Webb

Article points

1. Gestational diabetes (GD) is rare before 20 weeks of pregnancy.
2. Women who have experienced GD have an increased risk for future glucose intolerance, either by recurrent GD in future pregnancies or the development of type 2 diabetes at a later date.
3. Global screening strategies are not aligned, despite the increased prevalence of this condition, in part pre-determined by an increasingly obesogenic population.
4. GD is known to be more common in women from Asian and African-Caribbean populations, and recent studies suggest a higher risk to the offspring of mothers with GD than previously thought.

Key words

- Gestational diabetes
- Glucose intolerance
- Hyperglycaemia
- Pregnancy

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Gestational diabetes (GD) is defined as glucose intolerance first detected in pregnancy (World Health Organization, 1999), and is thought to affect 2–12% of all pregnant women (Department of Health, 2002). More recent research suggests that hyperglycaemia in pregnancy acts as a metabolic marker and, thus, contributes to future comorbidities for the offspring. Given the increasing prevalence of diabetes, alongside what has been described as an obesity epidemic, the potential for developing GD has never been greater. This article discusses the research surrounding GD, current recommendations relating to detection and treatment, and explores how GD might impact a multi-ethnic population.

Gestational diabetes (GD) usually presents in week 28 of pregnancy, and is rarely noted prior to week 20. If glucose intolerance is detected at this time it would usually indicate a glucose intolerant state that pre-dates the pregnancy, i.e. undiagnosed diabetes. The definition of GD applies irrespective of whether or not insulin is used in its treatment, or whether the condition does or does not remit post-birth.

GD affects 2–12% of all pregnant women (Department of Health [DH], 2002), but usually recedes after pregnancy. It is, however, an established marker both for future pregnancies to be complicated by GD and future maternal development of type 2 diabetes.

Background

GD involves maternal insensitivity to the action of insulin, probably due to the effects of placental hormones, together with an inability to make sufficient insulin, causing hyperglycaemia, which is transferred through the placenta to the fetus.

The fetus compensates for the elevated glucose level by increasing its production of insulin. This predisposes the storage of fat, which can lead to what is commonly known as macrosomia, defined variably as a birth weight of >4000–4500 g. Excess insulin production *in utero* can lead to neonatal hypoglycaemia, and there is a risk of breathing problems. The offspring of mothers who develop GD are thought to be at risk of developing obesity in childhood, and developing type 2 diabetes later in life (Dabelea et al, 2000).

GD deserves discussion as it has been shown to adversely affect both perinatal and maternal outcomes. The Pedersen (1952; 1954) hypothesis that "maternal hyperglycaemia results in excess transfer of glucose to the fetus resulting in fetal hyperinsulinaemia", has formed the basis of understanding the consequences of diabetes during pregnancy.

However, the degree to which intrauterine exposure to maternal hyperglycaemia of any severity, and the subsequent degree of responsibility this has for the development of future comorbidities, is in debate. It is postulated that any level of maternal hyperglycaemia acts as a metabolic marker and can therefore determine not only perinatal comorbidity but also future health outcomes for the offspring many years later (Keely et al, 2008; Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Cooperative Research Group, 2009).

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1. Possibly the greatest indicator of the need for clarification relating to the effects on fetal outcomes of any degree of maternal hyperglycaemia, together with the need for definitive recommendations for the detection and management of gestational diabetes (GD), is the proliferation of recent studies and articles to this effect.
2. The conclusions of ACHIOS (Australian Carbohydrate Intolerance Study in Pregnant Women) were that treatment of GD reduces serious perinatal morbidity and may improve the woman's health-related quality-of-life.
3. The HAPO (Hyperglycemia and Adverse Pregnancy Outcomes) study results indicated strong continuous associations of maternal glucose levels below those diagnostic of diabetes with increased birth weight and increased cord-blood serum C-peptide levels.

The increasing incidence of GD, together with an increase in the number of women with obesity, potentially has serious implications for the health of our nations in the very near future.

In England, in an effort to meet the standards set out in the National Service Framework for diabetes (DH, 2002), the National Clinical Director for Diabetes, Dr Rowan Hillson, has identified the need to improve pregnancy outcomes (including GD), as a key priority.

Possibly the greatest indicator of the need for clarification relating to the effects on fetal outcomes of any degree of maternal hyperglycaemia, together with the need for definitive recommendations for the detection and management of GD, is the proliferation of recent studies and articles to this effect. However, it also needs to be recognised that GD is under-diagnosed due to global differences in screening. Certain populations are more vulnerable to GD. Rates are higher in Asian populations than the white population and many women with previously undiagnosed type 2 diabetes are mis-diagnosed as having GD (Reece et al, 2009).

Recent research

The ACHOIS (Australian Carbohydrate Intolerance Study in Pregnant Women) trial assessed whether the treatment of GD would reduce perinatal complications and the effects of treatment on maternal outcomes, mood, and quality of life (Crowther et al, 2005). The study lasted 10 years, 1000 participants were enrolled and the intervention and control groups were of a similar size and characteristics at entry.

The results showed a lower incidence of perinatal complications in the intervention group compared with the group that received routine care (1% vs. 4%). Induction of labour was higher in the intervention group (39% vs. 29%) but the rates of caesarean birth were similar in the two groups. Three-month post-birth data revealed lower rates of depression and an indication of improved health status in the intervention group. Thus, the conclusions of ACHIOS were that treatment of GD reduces serious perinatal morbidity and may improve the woman's health-related quality-of-life (Crowther et al, 2005).

The US-based HAPO study was designed to clarify the risks of adverse outcomes associated with various degrees of maternal glucose intolerance less severe than that seen in overt diabetes (HAPO Study Research Cooperative Group et al, 2008).

The HAPO study results indicated strong continuous associations of maternal glucose levels below those diagnostic of diabetes with increased birth weight and increased cord-blood serum C-peptide levels. These results "when viewed together with those of the ACHOIS study indicate that maternal hyperglycaemia less severe than that used to define overt diabetes is related to clinically important perinatal disorders or problems and that their effects can be reduced by means of treatment, although a threshold for the need for treatment is not yet established" (HAPO Study Research Cooperative Group et al, 2008).

National guidance

In 2008, NICE published *Diabetes in Pregnancy: Management of Diabetes and its Complications from Pre-conception to the Postnatal Period* (National Collaborating Centre for Women's and Children's Health [NCCWCH], 2008). This document identifies the potential benefits of recognising and treating GD as including reductions in ill-health in the woman, the baby or both during, or immediately after, pregnancy, as well as the benefits of reducing the risk of progression to type 2 diabetes for the mother in the longer-term and future pregnancies being complicated by pre-existing diabetes or GD.

NICE recommends routine screening for GD at booking using the below criteria:

- BMI >30 kg/m^2.
- Previous macrosomic baby weighing ≥4.5 kg.
- Previous GD.
- First degree relative with GD.
- Ethnic origin at a high risk of developing diabetes.

If one of these is present then testing for GD should be offered using an oral glucose tolerance test (OGTT) at 24–28 weeks. According to a 1999 survey, 67% of UK maternity service providers currently screen using a combination of these factors (Aldrich et al, 1999). These criteria were chosen by the guideline development group

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1. In some groups, use of clinical risk factors misses nearly half the women with gestational diabetes (GD), and the performance of the screening method will depend on the maternal age, ethnicity, and BMI profile of each population.
2. Over the past 25 years, the UK has seen falling rates of fertility at younger ages alongside rising fertility rates at older ages. This has led to an increase in the mean age of childbearing, partly due to economic reasons and to older women wishing to conceive with a second partner.
3. GD should be treated initially with diet and exercise for 1–2 weeks. In women with a BMI of >27 kg/m^2, calorie restriction and moderate exercise is suggested. If near-normal blood glucose levels are not achieved by diet and exercise alone, or if ultrasound scans suggest fetal macrosomia, blood glucose-lowering therapy should be considered.

as the probability of a woman who has had GD in a previous pregnancy developing it again is 30–84%, and the probability of recurrent GD given insulin-treated GD in a previous pregnancy is approximately 75% (NCCWCH, 2008). In some groups, use of clinical risk factors misses nearly half the women with GD, and the performance of the screening method will depend on the maternal age, ethnicity, and BMI profile of each population (Chappell and Germain, 2008).

NICE did not include advanced maternal age as a risk factor for GD because this would result in most pregnant women receiving an OGTT. Over the past 25 years, the UK has seen falling rates of fertility at younger ages alongside rising fertility rates at older ages (Dunnell, 2007). This has led to an increase in the mean age of childbearing, partly due to economic reasons and to older women wishing to conceive with a second partner (Dunnell, 2007). However, the ACHOIS study provided evidence of potential benefit for treatment of even mild GD, and suggested that missing a substantial proportion of cases may translate into clinical detriment (Chappell and Germain, 2008).

Treating gestational diabetes

NICE (NCCWCH, 2008) recommended that GD should be treated initially with diet and exercise for 1–2 weeks. In women with a BMI of >27 kg/m^2, calorie restriction and moderate exercise is suggested. If near-normal blood glucose levels are not achieved by diet and exercise alone, or if ultrasound scans suggest fetal macrosomia, blood glucose-lowering therapy should be considered. The guidance suggests that clinically effective diabetes therapy includes oral antidiabetes drugs (metformin and glibenclamide) and insulin therapy using human insulin or rapid-acting insulin analogues, which should be tailored to the glycaemic profile of the individual and be acceptable to the woman.

Glycaemic targets for GD mirror those for women with pre-gestational diabetes and women should be asked to monitor their blood glucose levels pre- and 1 hour post-meal. The targets to aim for are fasting blood glucose levels of 3.5–5.5 mmol/L and a 1-hour post-meal glucose below 7.8 mmol/L (NCCWCH, 2008).

Women should be given all the available information and advice relating to the risks associated with GD and how they can be reduced with good glycaemic control, including management of diet and exercise. Blood glucose monitoring education and training needs to be robust enough to ensure that women understand its relevance and importance, rather than it simply being a task they are asked to perform. This needs to be approached sensitively so the woman understands the right balance between just getting a result and what that result means and why it is so important.

Advice relating to the birthing process should be offered, and the woman should be made aware that future pregnancies may be complicated by GD and that there is an increased risk of developing type 2 diabetes. However, a study by Kim et al (2007) suggests that, despite understanding the association between GD and post-partum diabetes, women with a history of GD usually did not perceive themselves to be at elevated risk.

Post-birth, if hyperglycaemia has remitted, all blood glucose-lowering therapy can be stopped. However, it is wise to continue to monitor blood glucose levels for 1 week to ensure that remittance has occurred. Following this it is usual to suggest that the woman has a further OGTT at 6 weeks, and further annual surveillance of glycaemic measurements.

Local experience

The area that Heart of England Foundation Trust serves is mainly covered by two PCTs: Birmingham East and North, and Solihull NHS Care Trust, both of which have markedly different populations and diabetes prevalences (*Table 1*).

Birmingham East and North PCT has a population of almost 450 000, 97% of whom are of non-white ethnic origin. All of the wards in the PCT are classified as urban. There is high economic deprivation – nine of the wards fall within the top 20% of the "most deprived" category, and 25% of the east of the borough has been labelled "least healthy" (Eastern Birmingham PCT, 2006).

Solihull NHS Care Trust has a mix of urban and rural communities, mostly white British

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1. According to the *Health Profile of England 2008* (Department of Health, 2009) Birmingham has an obesity prevalence of 23.4% in adults and 11.3% in children; similar data for Solihull gives the prevalences at 23.9% and 8.9%, respectively.
2. The major implications for primary care are that all women with gestational diabetes (GD) will need annual follow-up and to have the messages of the need for tight glycaemic control during pregnancy reinforced by their primary care providers, as many of these women underestimate the risk that GD poses.
3. The author has experienced a worrying disregard by women with GD for keeping antenatal appointments and undertaking rigorous blood glucose monitoring.

(94.6%). The more deprived communities are located in the wards in the north of the borough, but there are also pockets of deprivation seen in the south and west. Solihull NHS Care Trust has a population of approximately 220 000 and this population is mainly affluent (Solihull NHS Care Trust, 2008). There are pockets of deprivation in the north of the borough, but overall less than 5% of the population is classed as living in a deprived area. The incidence of diabetes is increasing in all age groups, which is associated with increasing levels of obesity. Predictive models suggest that if obesity continues to rise then diabetes prevalence could be as high as 5.05% by 2010 (Solihull NHS Care Trust, 2008).

According to the *Health Profile of England 2008* (DH, 2009), Birmingham has an obesity prevalence of 23.4% in adults and 11.3% in children; similar data for Solihull gives the prevalences at 23.9% and 8.9%, respectively. Both Solihull and Birmingham predict the prevalence of childhood obesity will rise further in line with national trends.

Given that women are choosing to try to conceive at an older age, and the increased prevalence of obesity which has already been identified as a risk factor for GD (along with maternal age), this is likely to pose a significant problem for the future.

Similarly, significant healthcare challenges exist in managing non-English speaking women with GD. It is well known that women from ethnic backgrounds face challenges in their pursuit of healthcare. They are difficult to reach via mainstream channels, and cultural or religious beliefs and lifestyles can affect healthcare delivery and management (Diabetes UK, 2006). Given the local ethnic populations, this will continue to impact on not only the author's services at Heartlands and Solihull hospitals, but also those delivered by primary care.

In a recent audit at Heartlands hospital, 68% of the audit population met the NICE criteria for GD screening in pregnancy (i.e. one or more risk factors). As discussed, Heartlands hospital serves a large ethnic population: 58% of the audit population are of south Asian descent, and 28% of the population had a first degree relative with diabetes. The other screening risk factors – BMI of ≥30 kg/m^2, previous macrosomic birth, and previous GD – were found to be less prevalent. Thus, 32% had no risk factors, 68% had one risk factor and 28% had two risk factors. If NICE guidance is to be followed, screening should be by means of an OGTT, which, based on an average antenatal clinic attendance of 93 women per week, will equate to over 3000 tests per annum.

A further audit was conducted by the diabetes specialist midwife of pregnancies complicated by diabetes at both sites (*Table 2*).

Table 1. Prevalence of diabetes and obesity in the author's local area (Quality and Outcomes Framework data for 2007/2008).

	Birmingham East and North	Solihull NHS Care Trust
Population	438 641	219 228
Number of practices	82	31
Number of people with diabetes	18 763	8398
Prevalence of diabetes	4.3%	3.8%
Prevalence of obesity	8.8%	8.0%

From: The Information Centre (2008)

The role of primary care

Clearly, the ethnic composition of populations will differ in other parts of the country from those in Birmingham – even within the author's locality there are two very different populations. However, as discussed, the incidence of GD is increasing, and as the prevalence of diabetes rises together with the levels of obesity, more women are going to develop GD. There is already evidence that childhood obesity is causing type 2 diabetes to be developed at an even younger age (Young et al, 2000) – is this the result of maternal glucose intolerance in gestation?

The major implications for primary care are that all women with GD will need annual follow-up and to have the messages of the need for tight glycaemic control during pregnancy reinforced by their primary care providers, as many of these women underestimate the risk that GD poses (Kim et al, 2007). The author has experienced a worrying disregard by women with GD for keeping antenatal appointments and undertaking rigorous blood glucose

monitoring. The author suggests that, given rising maternal age and the levels of obesity, increasing numbers of these women will need insulin therapy. It is therefore implicit that the risks associated with this therapy are balanced against the risks of maternal hyperglycaemia.

While most, if not all, of these women will be referred to and managed in secondary care, given the potential increase in numbers this may not be the case in the future. Practice nurses and GPs, therefore, need to ensure they have a broad knowledge of GD and the risks posed by maternal hyperglycaemia to the mother and fetus.

Recommendations

The ACHOIS and HAPO studies, and the evidence reviewed by NICE (NCCWCH, 2008), suggest a higher risk to the offspring of mothers with GD than previously thought. It therefore seems sensible to accept that any degree of intrauterine exposure to hyperglycaemia can predict morbidities later in life – currently observed as obesity in childhood and early development of type 2 diabetes. The results from the HAPO study could be used to develop criteria applicable to all women of child-bearing age (Metzger et al, 2009).

GD can itself serve as an indicator of future maternal glucose intolerance, and it has been shown that women who have had GD have a seven-fold increased risk of developing type 2 diabetes compared with those who have a normoglycaemic pregnancy (Bellamy et al, 2009). There is further suggestion that there needs to be some form of continuous assessment in GD, as the risk of developing overt diabetes seems to be maintained for many years (Lee et al, 2006; Bellamy et al, 2009). Further, increased lipid concentrations and blood pressure is estimated to confer a relative risk of aging 15 years, thus early identification and treatment of these factors could reduce premature cardiovascular and renal disease in this group (Bellamy et al, 2009).

Due to the fact that women with GD continue to underestimate the risks associated with this condition, the author believes that as healthcare professionals become more aware of the importance of managing hyperglycaemia in pregnancy, and as the incidence of GD increases due to the prevailing obesogenic society, positive health education messages need to permeate the public domain.

Table 2. Results of the local one-day diabetes audit.

Location	Type 1 (*n*)	Type 2 (*n*)	GD (insulin)	GD (metformin)	GD (diet)	Total
Heartlands	7	19	20	7	59	**112**
Solihull	0	3	18	0	11	**32**
Total	**7**	**22**	**38**	**7**	**70**	**144**

GD = Gestational diabetes

The role and importance of education for the woman relating to the risks associated with GD, together with the importance of blood glucose monitoring, cannot be underestimated. Although women with GD will not have experienced glucose monitoring as an intervention prior to their diagnosis, it is paramount that they are educated in relation to acceptable targets, encouraged to self-manage lifestyle adjustments and become proactive partners in their management.

The Confidential Enquiry into Maternal and Child Health are proposing a study to provide an overview of current practice nationally in post-pregnancy follow-up for GD. It aims to develop a local strategy of follow-up across the primary–secondary care interface, which will serve as the basis for a national model of best practice.

Walkinshaw (2002) identified that screening policies vary throughout the world (and all have deficiencies), and suggests that policies should be determined locally, as population and organisational issues will influence efficacy. Given the demographics of the population in eastern Birmingham the author concurs with this view.

Conclusion

The perspective of a woman with GD (*Box 1*) is quite prophetic and, while only one perspective, probably mirrors the feelings of other women with the condition. Healthcare providers are always challenged to take more notice of their patients, and the author believes that there is a need for more qualitative research in this area.

"The role and importance of education for the woman relating to the risks associated with gestational diabetes, together with the importance of blood glucose monitoring, cannot be underestimated."

Finally, it seems sensible to call on primary and secondary care providers, who undoubtedly have unrivalled knowledge of their populations, to develop robust strategies to ameliorate the risks for women with GD and their babies together with management and follow-up strategies that take account of increasing maternal age, prevalence of overt diabetes and the increasing levels of obesity. ■

Declaration of interest

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Box 1. The perspective of a woman with gestational diabetes.

"It was a shock being diagnosed – you don't expect it. I knew I was a little overweight, but didn't really think that it would be a contributing factor. I knew of diabetes, but didn't really know what it was or what it meant, or how to deal with it. To have to deal with gestational diabetes rather than enjoying pregnancy is a bit tough, but in some ways there is no choice. I didn't really discuss it with my family, and wasn't really made aware of what impact it would have on both my health and the baby.

I had a real fear of taking insulin, and first time round I went to the extreme to avoid it; my diet became restricted and I felt that I was managing it because my blood glucose levels were acceptable, but in hindsight did I do the right thing? If I had known what I know now about diabetes I think it would have put me off having children. I had questions about the future: how would it affect any future pregnancies? What would it mean for the labour? Would the child be ok? Would it have diabetes? I wasn't so bothered about having to monitor glucose regularly, and in some ways it was reassuring when the monitoring was OK because I knew I was doing the right thing. It did medicalise the pregnancy, but I knew no different, and in some ways it was reassuring that I was getting a lot of care.

The second time around I was annoyed that I developed gestational diabetes again, but as I had information and knowledge I was able to control it better. Although I went through similar feelings I felt more in control."

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