

Inadequate post-partum screening for type 2 diabetes in women with previous gestation diabetes mellitus: a retrospective audit of practice over 17 years

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What's already known about this topic?

Gestational diabetes mellitus (GDM) represents the largest risk factor for the development of type 2 diabetes mellitus (T2DM) and affects approximately 5-10% of pregnancies.

It has long been recommended that women with GDM be assessed for hyperglycaemia shortly after delivery and in the long term. In the UK, this was adopted into national guidance by the National Institute of Health and Care Excellence (NICE) in 2008.

What does this article add?

Despite being high risk for developing T2DM, it was found that many women with a history of GDM were not tested for the condition at the frequency outlined in guidance.

During long-term follow-up, we demonstrated a significant trend showing declining rates of testing with an increase in time from delivery.

We showed that 38% had results consistent with diabetes by 10 years post-partum and that testing within the first year was linked to an increased likelihood of detecting hyperglycaemia in the early years, emphasising the importance of regular screening.

ABSTRACT

Introduction: Women with gestational diabetes (GDM) are at greatly increased risk of type 2 diabetes (T2DM).

The UK guidance recommends screening for T2DM at around 6 weeks post-partum and annually thereafter.

We evaluated conformity to this guidance in two separate time periods.

Methods: The proportion of tests performed within guidance was assessed using longitudinal plasma glucose and glycated haemoglobin data in two cohorts (1999-2007, n=251; 2015-2016, n=260) from hospital records on women previously diagnosed with GDM.

Results: In the 1999-2007 and 2015-2016 cohorts, 59.8% and 35.0% of women had the recommended post-partum testing, respectively ($p<0.001$); just 13.5% and 14.2%, respectively, underwent the first annual test on time. During long-term follow-up of the 1999-2007 cohort (median follow-up: 12.3 years), the proportion of women tested in any given year averaged 34.2% over a 17-year period; there was a progressive decline in the proportion of women receiving a yearly test with time since delivery ($p=0.002$).

Over the follow-up period, 85 women from the 1999-2007 cohort developed blood test results in the diabetic range with a median time to presumed DM diagnosis of 5.2 years (range 0.11-15.95 years). Kaplan-Meier analysis showed that 18.8% of women had blood test results in the diabetes range by 5 years and 37.8% by 10 years post-partum.

Conclusions: Despite high profile guidelines and a clear clinical rationale to screen women with a past diagnosis of GDM, many women did not receive adequate screening for T2DM, both in the short- and long-term. This suggests alternative approaches are needed to ensure effective follow-up of this high-risk group. To have an impact, interventions need to be tailored to a young, generally healthy group in which traditional approaches to follow-up may not be best suited.

Key Words

gestational diabetes mellitus; follow-up; screening; diabetes mellitus, type 2

List of abbreviations: DM; diabetes mellitus, FPG; fasting plasma glucose, GDM; gestational diabetes mellitus, HbA1c; glycated haemoglobin, HR; hazard ratio, IQR; inter-quartile range, NICE; National Institute for Health and Care Excellence, OGTT; oral glucose tolerance test, RPG; random plasma glucose, SD; standard deviation, T2DM; type 2 diabetes mellitus

INTRODUCTION

Gestational diabetes mellitus (GDM) represents the largest risk factor for the development of type 2 diabetes mellitus (T2DM) and affects approximately 5-10% of pregnancies [1,2]. It is more likely to develop in women who have risk factors, which include: non-Caucasian ethnicity; obesity; a family history of diabetes; previous GDM and previous macrosomic baby [3]. GDM can result in adverse metabolic sequelae for both mother and baby. In mothers with GDM, 35–60% will develop T2DM within 10–20 years post index pregnancy [4-8]. Indeed, a meta-analysis reported women with GDM were seven-fold more likely to develop subsequent T2DM than women with normoglycemic pregnancies [8].

The monitoring of women with a history of GDM for future dysglycaemia and early intervention is therefore important in this young, generally healthy population, particularly in view of the availability of effective interventions. For example, the Diabetes Prevention Program follow-up study showed that, in women with impaired glucose tolerance, intensive lifestyle intervention or metformin reduced the risk of developing diabetes by 35% and 40% respectively [9]. Thus, it has long been recommended that women with GDM be assessed for hyperglycaemia shortly after delivery and in the long term [6,10,11]. In the UK, this was adopted into national guidance by the National Institute of Health and Care Excellence (NICE) in 2008 [12], followed by an update in 2015 [13]. This latest guideline stipulates that a follow-up fasting plasma glucose (FPG) be offered at 6-13 weeks post-delivery followed by annual testing thereafter, using glycated haemoglobin (HbA1c), to screen for T2DM.

The aims of this study were to evaluate long-term conformity to local and national screening guidance in women with previous GDM. We examined both immediate post-partum glycaemia testing and long-term repeated annual follow-up over a 17-year period. To our knowledge there are no published studies examining longitudinal follow-up testing over this extended period of time.

METHODS

Participant

1999-2007 cohort:

Women diagnosed with GDM by antenatal oral glucose tolerance test (OGTT) were identified between July 1999 and January 2007 at the University Hospitals of North Midlands as part of an audit (n=251; median age at delivery=31 years [IQR 27-35 years]). Details of these cases have been published previously [14]. During this period, GDM was diagnosed by OGTT results using a local protocol in use at the time (a modified version of the WHO[1999] criteria; OGTT cut-offs: fasting ≥ 6.1 mmol/L, 2 hour ≥ 7.8 mmol/L).

2015-2016 cohort:

In a separate audit, performed at the same centre following the introduction of the 2015 updated NICE guideline, women diagnosed with GDM by antenatal OGTT were identified between March 2015 and February 2016 (n=260; median age at delivery=32 year [IQR 28-36 years]). For this group a diagnosis was made using the NICE 2015 criteria (OGTT cut-offs: fasting ≥ 5.6 mmol/L, 2-hour ≥ 7.8 mmol/L).

All data were collected and analysed as a clinical audit of practice against guidance. Therefore, ethical approval was not required.

Data collection

Using the 1999-2007 cohort, retrospective data from clinical laboratory records were utilised to document testing of post-partum glycaemic status for the period from date of delivery until September 2016 (median follow-up: 12.3 years; range: 9.5-17.1). These data included dates and results of random plasma glucose (RPG), fasting plasma glucose (FPG), HbA1c and OGTT investigations and were used to determine (i) whether women had the recommended immediate post-partum tests (recommended at 6 weeks as per local protocol at the time of the study), (ii) annual screening tests and (iii) the potential development of T2DM. For the purpose of this study, women were considered to have developed T2DM if they had at least one of: RPG ≥ 11.1 mmol/L, FPG ≥ 7.0 mmol/L, HbA1c ≥ 48 mmol/mol (6.5%) or 2-hour test on OGTT of ≥ 11.1 mmol/L. During the time period the data collection spanned (1999-2016), NICE 2008 guidelines were introduced which

recommended a 6-8 week post-partum FPG following delivery and an annual test thereafter [12] allowing us to assess the impact of this guidance change on monitoring patterns.

For the 2015-2016 cohort, the same approach was used to collect post-partum testing data for a follow-up period of 60 weeks post-delivery. Data were used to assess whether women had the recommended post-partum FPG at 6-13 weeks as well as an assessment of glycaemic status at 1 year.

Statistical analysis

All statistical analyses were performed using Stata (version 14; College Station, TX). Chi-squared tests were used to compare differences in categorisation describing whether time from delivery to the first post-6 week test was on time or not, and in proportions of patients who developed DM. Cox's proportional hazards regression was used to examine factors associated with time from delivery to development of DM. Kaplan-Meier plots were used to illustrate these data visually. Assessment of the 6-week post-partum test was allowed a tolerance of 2 weeks (i.e. 4-8 weeks) while the annual follow-up testing was allowed a tolerance of 2 months (i.e. 44-60 weeks). To assess annual testing rates over time the extended Mantel-Haenszel chi-square test for linear trend was utilised (OpenEpi, Version 3).

RESULTS

Conformity to guidance on 6-week post-partum testing

We first determined the proportion of women who had the recommended 6-week post-partum FPG test. Of the 251 women diagnosed with GDM from 1999 - 2007, 150 (59.8%) had the 6-week (± 2 weeks) post-partum FPG (Table 1a). Of the 101 women who did not have testing in line with this standard, the majority (100) did not have a FPG prior to 8 weeks (i.e. too late); just one patient was tested too soon (before 4-weeks post-partum).

To evaluate testing rates in a more recent cohort, we determined the proportion of women diagnosed with GDM in the 12 months from March 2015 to February 2016 who underwent immediate post-partum testing (fasting FPG) within the revised NICE 2015 recommend time frame of 6-13 weeks post delivery. Of the 260 women in this group, 91 (35.0%; (Table 1b) had testing performed in line with this standard, a clear reduction in testing rates compared to the historical cohort ($\chi^2_1 = 31.4$; $p < 0.001$).

Conformity to guidance at 1 year post-partum

Overall, in the 1999-2007 cohort, only 34 of the 251 women (13.5%) had a follow-up FPG at 52 ± 8 weeks, though a larger proportion (104/251; 41.4%) had a test at some point prior to 60 weeks. Of the 150 tested at 6 ± 2 weeks post-partum, only 15.3% had the subsequent annual test at the recommended time (44-60 weeks), while 20.7% were tested too soon (9-43 weeks) and the remaining 64.0% were tested too late (>60 weeks or not at all) (Table 1a). By comparison, of the 101 women who did not have a post-partum test within 8 weeks of delivery, the proportion who had the recommended annual test (44-60 weeks) was lower, at only 10.9%, while those tested too soon was higher, at 38.6%, and those tested too late lower, at 50.5% ($\chi^2_3 = 9.73$, $p = 0.008$) (Table 1a). In the 133 women tested at 6 ± 2 weeks post-partum who had further follow-up testing, the median time from delivery to first post 6-week test was 1.34 years (IQR 0.75-2.28). For the 94 women who did not have the post-partum test at 6 ± 2 weeks but did have at least one follow-up investigation after this time, median time to first test was 1.17 years (IQR 0.54-3.18). The difference between the median times was not significant ($p = 0.937$).

In the 2015-2016 cohort, 14.2% (37/260) of women with a previous history of GDM had an assessment of glycaemic status at 1 year (44-60 weeks); similar to the 1999-2007 cohort. The proportion that had some form of testing for diabetes (HbA1c and/or FPG) within 1 year (<60 weeks) was larger, and comparable with the 1999-2007 cohort at 40.4% (105/260). Of the 169 women in the 2015-2016 cohort who had not been tested in the post-partum period, 23/169 (13.6%) were tested at 52±8 weeks, similar to the proportion who had been tested at 6-13 weeks (15.4%). Proportions tested too soon (25.4% and 27.5%) and too late (61.0% and 57.1%) were also similar between the two groups, such that the overall distribution was not significantly different ($p=0.832$) between those who were and those who were not tested in the immediate post-partum period (Table 1b).

Conformity to long-term annual testing

To evaluate long-term annual testing rates, we used the 1999-2007 cohort to determine the proportion of patients who had at least one test in each calendar year. As shown in figure 1a, the proportion tested remained between 25% and 40% over the follow-up period (mean±SD: 34.2±4.9%). The introduction of the first NICE guidance in 2008 did not appear to influence testing rates; mean proportion receiving an annual test for the periods pre-2008 and post-2008 did not differ (33.7% and 34.1%, respectively; $\chi^2_1=0.03$, $p=0.871$). When annual testing levels were assessed in terms of years since delivery, there was a significant trend for a lower rates of testing when a greater amount of time had elapsed (Extended Mantel-Haenszel chi square for linear trend=9.89; $p=0.002$) (Figure 1b).

Development of type 2 diabetes

In total, over the follow-up period, 85 women from the 1999-2007 cohort developed blood test results in the diabetic range with a median time to presumed DM diagnosis of 5.2 years (range 0.11-15.95 years). Kaplan-Meier analysis showed that 18.8% of women had blood test results in the diabetes range by 5 years and 37.8% by 10 years post-partum.

Many of the women who had testing at 6-weeks post-partum received this in the form of a 2-point OGTT. Of the 150 women tested, five had a FPG ≥ 7.0 mmol/l and a further two had a 2-hour plasma glucose of ≥ 11.1 mmol/L (FPG 5.0 and 6.8 mmol/L), indicating seven cases (4.7%) of likely DM in the immediate post-partum

period. Using Cox's proportional hazards regression, the time to development of likely DM was not significantly different between those tested at 6 weeks and those not ($p=0.352$, $HR=1.24$, $95\% CI=0.79-1.93$) (Figure 2a). For those with no 6-week testing, the proportion with DM at 2 and 5 years were 5.5% and 18.5%, respectively, compared with 10.2% and 19.0%, respectively, for those who were tested at 6-weeks.

Similarly, the overall time to development of likely DM was not statistically different ($p=0.359$, $HR=1.29$, $95\% CI=0.75-2.25$) between those who had a follow-up test within the first year (≤ 60 weeks groups combined), compared with those who did not have a test within this time (>60 week group). However, the Kaplan-Meier plot (Figure 2b) suggests that the group who had a follow-up test within the first 60 weeks demonstrated a higher proportion with likely DM in the early years (10.4% and 14.5% after 2 and 3 years, respectively), compared with those who did not have a test within one year (0.0% and 4.4% after 2 and 3 years, respectively). This may reflect missed opportunities to diagnose DM early in the years soon after delivery, highlighting the importance of regular testing during this period.

DISCUSSION

Despite being high risk for developing T2DM, it was found that many women with a history of GDM were not tested for the condition at the frequency outlined in guidance. In the 1999-2007 cohort, only 59.8% of women were tested at 6 weeks post-partum, and this had deteriorated by the time of collection of the 2015-2016 cohort to 35.0%. In both cohorts, the only a minority were tested around the first anniversary of delivery (1997-2007 cohort: 13.5%, 2015-2016 cohort: 14.2%). When long-term testing rates were examined in the 1999-2007 cohort, the proportion of patients who had at least one test in any given year was consistently low (mean: 34.1%). Furthermore, we demonstrated a trend for reduced rates of testing with an increase in time from delivery. Reflecting their elevated risk of T2DM, of the patients tested, many had results consistent with diabetes (33.7% over the follow-up period), emphasising the importance of regular screening.

The sample sizes for both cohorts were relatively small and the patients were all from the same local area. Therefore, our data may not be representative of practice at a national or international level. However, given our findings are consistent with other studies investigating follow-up to one-year post-partum [15, 17-21], it is reasonable to assume that the consistently low testing rates in the years beyond this initial period, as our study demonstrates, may reflect practice in other geographical areas.

Consistent with our data, short-term post-partum testing rates described in the literature are generally poor [15, 17-24], but variable, with one systematic review demonstrating levels ranging from 34% to 73% [15]. Compared to the literature, the short-term testing rates in our study, though suboptimal, were higher in the 1999-2007 cohort than described in many studies (59.8% tested at 6(\pm 2) weeks post-partum). One study from the United Kingdom showed testing at 6-weeks to be 45% [22] (and hence more comparable to our 2015-2016 cohort) and another just 18.5% within 6 months. Interestingly, this latter study identified significant regional variation within the UK [17]. In a study using a questionnaire, self-reported post-partum testing amongst UK primary care physicians was 80%, though this may be an overestimate due to the self-reporting methodology employed [24]

McGovern et al [17] demonstrated that long-term annual rates were typically around 20% across a five-year period from 2006 to 2010 and, as demonstrated for the short-term, this varied significantly across English

regions. Unlike our findings that testing levels reduced with time since delivery, McGovern et al did not find time since diagnosis to be a predictor of long-term follow-up. However, our data suggest that the most apparent reduction in testing rates did not occur until at least 10 years post-delivery, which would not have been detected in the follow-up period covered by McGovern et al [17]. A number of studies have demonstrated the lack of impact new clinical guidance has had on the uptake follow-up testing [17, 22, 25, 26], as we showed with regard to the NICE 2008 guidance in this study, and have shown previously in other diabetes settings [27].

The proportion of patients diagnosed with likely DM in our study (18.8% by 5 years, 37.8% by 10 years) was in line with those determined in other work [5], including a relatively recent UK-based study that established a definitive diagnosis from a comprehensive diabetes clinical information system [28]. The systematic review by Kim et al. showed a relatively high incidence of T2DM in the first 5 years after delivery with an apparent plateau from 10 years [5]. This is largely consistent with our findings, and reaffirms the need for regular testing, particularly in the first decade from delivery. The impact of screening tests on rate of detection of DM, while not statistically significant overall in our data, suggested that there may be missed opportunities to diagnose DM early in the years soon after delivery, highlighting the importance of regular testing during this period.

Despite clear national guidance on when to screen women with a history of gestational diabetes for the development of T2DM, there appears to be some uncertainty amongst healthcare professionals as to who is responsible for arranging the necessary investigations for this, both in the short and long term. Pierce et al explored the practice of UK healthcare professionals with respect to follow-up in patients post-GDM and found that there is confusion between primary and secondary care as to who is responsible for follow-up with fewer than 40% of GDM follow-up protocols agreed across both primary and secondary care [24]. This was compounded by the sense that post-GDM follow-up was not a high priority and difficulties in effectively communicating the original GDM diagnosis to general practitioners. This is consistent with our own experience and similar findings have been reported by Shah et al in a Canadian population [20]. This cohort study found that although the majority of women with GDM had post-partum visits with a family physician or obstetrician, fewer than one in six women received a post-partum OGTT within six months of delivery [20].

This highlights that urgent action is required to clarify key issues of responsibility, communication and prioritisation in this high-risk group of women.

In addition to those associated with healthcare providers, there are also factors from the perspective of the patient that pose potential barriers to testing. The DIAMIND trial identified that the common barriers to testing were not having enough time, inadequate childcare provision, and prioritising the health of the baby [29]. This study also highlighted the preferred way for receiving reminders for post-partum screening was SMS. Using mobile technology has recently been proposed as a possible tool for improving follow-up post-GDM and reducing the development of T2DM in the UK. It is essential that such systems should be designed with the views and experience of post-GDM patients taken into account [30].

Strengths and limitations

The strength of our retrospective study is the long period over which data were collected for the 1999-2007 cohort, coupled with more recent cohort, allowing comparison of screening behaviour over time in both annual (for up to 17 years post-delivery) and post-partum testing. To our knowledge, this is the longest follow-up period for a study addressing this topic. In the 2011 systematic review by Tovar et al [15], none of the studies evaluated screening rates beyond one year post-partum, with the exception of one study evaluating an Australian GDM registry which provided women with annual mail reminders [16]. More recently, a UK based study looked at long-term follow-up, but only over a period of 5 years [17].

Data on the 1999-2007 cohort was initially collected as part of a separate audit and therefore did not include all women with GDM over that time period. Furthermore, we did encounter difficulties in collecting all relevant baseline information from clinical records and hence some cases were excluded from the final analysis. Ideally, we would have preferred a more focussed cohort collected over 1-2 years (which we were able to do for the 2015-2016 cohort). However, the 1999-2007 group of women provided the unique opportunity to explore long-term screening behaviour. While a prospective study design would have been preferable, this would have been challenging to follow up for such a protracted period of time

4.5 Conclusions

Despite high profile guidelines and a clear clinical rationale to screen women with a past diagnosis of GDM, many women did not receive adequate screening for T2DM, both in the short- and long-term. This suggests alternative approaches are needed to ensure effective follow-up of this high-risk group. To have an impact, interventions need to be tailored to a young, generally healthy group in which traditional approaches to follow-up may not be best suited.

Declaration of interests:

None.

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Tables

Table 1a. Post-partum glycaemic status testing in women with GDM (1999-2007 cohort).

	Not tested at 6(±2) weeks	Tested at 6(±2) weeks	p	χ^2_2
<u>6-week postpartum test</u>	101/251 (40.2%)	150/251 (59.8%)		
<u>Subsequent test*:</u>				
At 1 year (44-60 wks)	11/101 (10.9%)	23/150 (15.3%)		
Before 1 year (9-43 wks)	39/101 (38.6%)	31/150 (20.7%)	0.008	9.73
Over 1 year (>60 wks)	51/101 (50.5%)	96/150 (64.0%)		

*Excludes initial 8 week post-partum period

Table 1b. Post-partum glycaemic status testing in women with GDM (2015-2016 cohort).

	Not tested at 6-13 weeks	Tested at 6-13 weeks	p	χ^2_2
<u>6-13-week postpartum</u>	169/260 (65.0%)	91/260 (35.0%)		
<u>test</u>				
<u>Subsequent test*:</u>				
At 1 year (44-60 wks)	23/169 (13.6%)	14/91 (15.4%)		
Before 1 year (14-43 wks)	43/169 (25.4%)	25/91 (27.5%)	0.832	0.37
Over 1 year (>60 wks)	103/169 (61.0%)	52/91 (57.1%)		

*Excludes initial 13 week post-partum period

Figure legends

Figure 1. Proportion of annual tests performed each year (1997-2007 cohort).

Proportion of women who had at least one test for (a) each full calendar year of the follow-up period, and (b) each year since date of delivery. Excludes testing performed after the finding of an abnormal glucose/HbA1c result.

Figure 2. Kaplan-Meier plots showing development of DM (1997-2007 cohort).

Development of test result within the diabetes range for (a) patients who had 6-week post-partum testing compared to those that did not and (b) patients who had testing within 60 weeks compared to those that did not.