Gestational diabetes and progression to type two diabetes mellitus: missed opportunities of follow up and prevention?

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Abstract

Background: The incidence of type 2 diabetes (T2DM) is increasing. Having a pregnancy complicated by gestational diabetes mellitus (GDM) is a potent risk factor for the later development of T2DM.

Aims: To explore the characteristics of women diagnosed with GDM in a single centre and their follow up for progression to T2DM.

Methods: A retrospective cohort study using anonymised data of one hundred and fifty four (154) women with GDM receiving maternity care at the Oxford University Hospitals NHS Foundation Trust (OUHFT) in 2010 and their follow up until 2018.

Results: The prevalence of GDM in women delivering in Oxfordshire in 2010 was 3.4%. 70% of pregnant women were overweight or obese (with 51% being obese) at booking. Gestational weight gain (GWG) was excessive in 29% of women, when compared to Institute of Medicine (IOM) guidelines. Almost a quarter of women (23.4%) had no follow up after delivery. Over a median follow up of 3.5 years (range 0-8 years) nearly one in six (16.9%) of the total cohort (22% of those tested) went on to develop T2DM. 74% of women with GDM were multiparous, and 65% of nulliparous women were tested compared to 81% of multiparous women. There was a significant difference between multiparous women (53.8%) compared to nulliparous women (46.2%) developing T2DM ($p=0.01$). There was no significant difference in BMI ($p=0.866$) or GWG ($p=0.83$) in women who progressed to T2DM versus those who did not.

Conclusion: The risk of T2DM after GDM is substantial however, follow up rates of this population is poor. Subsequent screening of women with GDM and their management

crosses secondary and primary care with scope for improvement in counselling of women of the importance of annual reviews, in data collection and follow up in both obstetrics and general practice. The implementation of a recall system, an education programme for general practitioners and/or a registry of women diagnosed with GDM could be useful to identify those at high risk of developing T2DM as well as providing a platform for the potential development of interventions to prevent progression to T2DM after GDM.

Highlights:

1. **The incidence of type 2 diabetes is increasing.**
2. **Gestational diabetes is a potent risk factor for T2DM.**
3. **Follow up of women with gestational diabetes is inadequate.**
4. **Establishing active recall screening and implementation of interventions may help.**

Introduction

GDM is glucose intolerance which is first diagnosed during pregnancy. In the United Kingdom (UK) and worldwide, prevalence has increased dramatically over the last 10 years with an estimated prevalence of 20% in the UK in 2019 [1]. This is in part due to more inclusive screening policies and stringent diagnostic criteria. In the 2008

Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study, adverse outcomes were reported at lower levels of hyperglycaemia than previously described [2]. In response the International Association of Diabetes and Pregnancy Study Groups (IADPSG) suggested new diagnostic criteria for GDM [3], which were adopted by the World Health Organisation (WHO) in 2013 [4].

Current NICE guidelines [5] advise targeted screening for GDM, however the thresholds for diagnosing GDM differ from WHO [4] and IADPSG [3] guidance (Table 1). NICE advocate screening in at risk populations including women with a body mass index (BMI) ≥ 30 kg/m², women with a family history of diabetes, or a previous history of GDM, women who have previously delivered a baby weighing > 4.5 kg, and women with minority ethnic family origin with a high prevalence of diabetes [5].

30% of women in England are obese (BMI ≥ 30 kg/m²) [6]. UK data from 2017 indicate that at booking 21.3% of pregnant women were obese (BMI≥ 30kg/m²) and less than a half (47.3%) had a normal BMI (<25 kg/m²) [7]. There is a strong association between maternal obesity and GDM [8]. Maternal obesity is also associated with adverse cardio-metabolic outcomes throughout the lifetime of the offspring, including higher childhood BMI, higher adult BMI, and increased risk of coronary heart disease and stroke [9]. Specifically, GDM increases the risk of hypertensive disease in pregnancy, pre-term labour, caesarean section, and large for gestational age babies [10]. It is not well understood to what extent GDM, booking BMI and/or GWG contributes to these complications.

NICE recommends pregnant women are weighed and BMI calculated at booking. It does not suggest giving advice on weight goals, however it recommends a dietician referral in women with BMI ≥30kg/m², but only repeat weighing if clinically indicated [11]. The American Institute of Medicine (IOM) in 2009, issued guidelines on GWG according to pre-pregnancy BMI [12] (Table 2). Meta-analysis has reported GWG below the recommended IOM range according to pre-pregnancy BMI can improve outcomes [13]. Including reductions in large for gestational age babies and caesarean section rates, but can increase the risk of small for gestational age babies, therefore GWG within guidelines but not below should be encouraged [13].

The association between GDM and T2DM is well established [14, 15]. This risk is highest in the first five years after pregnancy, and up to 70% of women will transition to T2DM [15].

The aim of this study was to establish the incidence and characteristics of pregnant women with GDM in Oxfordshire in 2010 and their subsequent follow up until April 2018 to determine how many women received appropriate follow up and how many developed T2DM.

Method

Research design

A retrospective cohort design was used to compare characteristics of women diagnosed with GDM, including age, booking BMI (kg/m²), parity, GWG, ethnicity and follow-up for the development of T2DM. Anonymised data were retrieved from the OUHFT maternity and laboratory databases, from the index pregnancy in 2010 to 2018.

Study population

All records for women who delivered at OUHFT in 2010 were searched for inclusion in the study. Women who were diagnosed with GDM in antenatal clinics and referred to OUHFT before delivery were identified, by searching for the ICD-10 code for GDM. Using the maternity unit database, information including booking weight and height, parity, twin pregnancy or not, ethnicity, and last weight recorded for each woman were collected. The laboratory database was then searched for associated blood tests including oral glucose tolerance test (OGTT), fasting plasma glucose and glycated haemoglobin (HbA1c) from 2009 to 2018. The two data sets were merged and anonymised. The data were examined. BMI at booking and GWG were calculated using height, booking weight and last weight recorded. T2DM diagnosis was confirmed by blood results including OGTT and HbA1c [16, 17]. The number of years follow up was calculated using the final year a blood test was recorded from the index pregnancy or the year a diagnosis of T2DM was made.

Ethical approval

The study was conducted using NHS data and was approved by the University of Chester, Faculty of Medicine, Dentistry and Life Science Research Ethics Committee (1391/18/EW/CSN), the Health Research Authority (18/HRA/0991, IRAS project ID: 240998), and OUHFT Trust Management Approval (R&D: 13607).

Patient and public involvement

There was no active patient involvement in this database review study.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences version 23 for Windows (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). Characteristics of women with GDM were analysed using descriptive statistics (mean for continuous variables and proportions for categorical variables). In addition BMI was treated as a categorical variable and grouped into normal weight, overweight and obese, using NICE guidance for ethnic groups [18], and GWG calculated and characterised as excess or not, according to Institute of Medicine (IOM) guidelines for each BMI category [12]. Women were grouped into five ethnic categories: White, Asian, Black, Chinese and other. Data were tested for normality using the Kolmogorov Smirnov test. Maternal age at diagnosis and booking BMI were normally distributed. Independent t-tests were used to test for differences between women who developed T2DM and those that did not. Chi square tests were used for categorical variables. A value of $p \leq 0.05$ was considered significant.

Results

In 2010, 5719 women gave birth at OUHFT and 192 were coded as having GDM (as per IADPSG diagnostic thresholds), giving a prevalence of 3.4%. However, 38 were excluded due to missing or anomalous data. The data from 154 women were included in the study. All pregnancies resulted in live babies, and there were three twin pregnancies. The median number of years follow-up of women with GDM was 3.5 (range 0-8 years).

At delivery, the age of women ranged between 19 and 43 years with a mean of 32 years (SD 5.42 years); 26 (16.9%) women developed T2DM (see table 3).

Just over half of women (50.6%) were obese at booking, and mean BMI at booking was 30.5kg/m² (ranging between 18.8 and 48.9kg/m²) (see table 3). Further analysis revealed 21 women (13.6%) had BMI ≥ 40kg/m². Height or weight data was missing at booking in 13 women (8.5%) for whom BMI could not be calculated.

Most women (70%) were ethnically White, 22% Asian, 9.7% Black, 2.6% Chinese and 3.2% other, representing the local demographic. There were significant differences between booking BMI and ethnic group; 80% of Black women, 56.7% of White women and 40% of Asian women were obese at booking (p=0.004).

Just over half of women (50.6%) had a measurement for glycaemia within 13 weeks of delivery. Although NICE has recommended since 2015[5] that the measurement of HbA1c can be used as the follow up test this was only carried out in 7.8% of women. Almost a quarter of women (23.4%) with GDM had no follow up. 33% of Black women, 25% of Other women, 20% of White women and 18% of Asian women were lost to follow up compared to 100% of Chinese women (p=0.05). Nulliparous women (35%) were more likely than multiparous women (19%) to be lost to follow up (p=0.43).

Nearly one in six (16.9%) of the total cohort went on to develop T2DM. Of the women with GDM who progressed to T2DM over the study period, diagnosis occurred during the first three years after the index pregnancy in 53.8%.

GWG was considered excessive according to IOM guidelines for each grouping of pre-pregnancy BMI [12]. Forty-five (29.2%) women were categorised as having excessive GWG. Excessive GWG was significantly related to booking BMI category (p = 0.006), as women obese at booking were more likely to have excessive GWG (see table 3). While

27% of the women who subsequently developed T2DM had excessive GWG, this was not significant (p=0.828).

Discussion

The prevalence of GDM among pregnant women in Oxfordshire in 2010 was 3.4%. This is similar to results from elsewhere in Europe where the prevalence at this time was 2-6% [19], but with new guidance, screening protocols and diagnostic criteria, prevalence has increased and current estimated prevalence for the UK is 20% [1]. Women who were obese at booking were more likely to have excessive GWG. Nearly one in six (16.9%) of the total cohort went on to develop T2DM. Being primiparous, over-weight or obese and having excessive GWG increases the risk of post pregnancy weight retention [20, 21] and this is associated with a nearly 1.5 increase in risk of developing T2DM [22]. In comparison our study had a short follow up period that did not measure postpartum weight retention.

Although this study did not report a significant relationship between obesity and progression to T2DM there was a high prevalence of obesity in our study population (51%). This compares to 21.3% of women being obese in 2017 at booking [7]. Consequent to the increasing prevalence of obesity it is likely that GDM and related T2DM will further increase in the future with associated cost implications. A recent study reported that being overweight or obese was a greater risk than genetic predisposition or an unhealthy lifestyle in developing T2DM [23] . There are currently 3.8 million people with diagnosed diabetes in England, accounting for 10% of the health budget [24]. Many studies report that GDM burdens women with a 70% lifetime risk of T2DM [15]. A study from the UK utilising a primary care data base found that women with GDM were

over 20 times more likely to develop T2DM over 26 years follow up [25].This large (9118 women with GDM) cohort study using primary care data from the UK reported postnatal screening in 58% of women in the first year and annual rates declined thereafter [25]. In contrast, our screening rate in the first year after delivery was 76.6%, however the transition rate was lower which may be a reflection of the short data collection period.

Along with increased risk of T2DM, women with GDM have an increased risk of future ischaemic heart disease (IHD) and hypertension [25]. The common risk factor is obesity, and while there are currently no recommendations for screening for IHD and hypertension after GDM, it is difficult to see how healthcare services could implement this additional screening requirement successfully in view low levels of follow up for T2DM.

NICE recommends that women with GDM should be followed up and tested to exclude T2DM by blood glucose testing soon after delivery, a postnatal fasting plasma glucose by 13 weeks (or HbA1c if after 13 weeks), and an annual HbA1c thereafter [5]. Lack of time has been identified as a barrier which hinders follow up by primary care physicians [26]. The HbA1c blood test is a single test that does not require a fasting blood test or repeat blood tests at one and two hours. Consequently an annual HbA1c test is a practical and less time consuming alternative to OGTT, and may improve uptake of screening and should be the test of first choice [5].

Australia set up a national database for GDM in 2011 [27] and a proactive system for recall and follow up. An evaluation of the scheme has shown high rates of non-mandatory registration (86-97%), and screening rates in the postpartum period of 43-58%, but no improvement in long term follow up [28].

Women's awareness of the risks of developing T2DM after GDM is high, but they do not always perceive themselves as personally being at high risk and up to 7% do not perceive any risk [29]. Women report the transitory nature of GDM as emphasised by healthcare professionals providing false reassurance, and acting as a barrier to risk perception and possible lifestyle interventions [30]. Primary care physicians need to improve knowledge of local guidelines and implement robust recall and reminder systems [25, 26].

Limitations

This study is limited by small numbers and a short follow up (median 3.5 years), however it is relevant to everyday primary care. The data in this study did not include previous history of GDM which is a potential confounding factor. Information was not available on women who subsequently moved from the Oxford region and were lost to follow up. Additionally there was no information on how GDM was treated (lifestyle, metformin or insulin), advice about and uptake of breast feeding [31], and future lifestyle including diet and exercise as these can potentially slow progression to T2DM [32].

Conclusion

This study has shown that the prevalence of GDM in Oxfordshire was 3.4% in 2010. 16.9% of women tested in the postnatal period progressed to T2DM during a median of 3.5 years, but a significant proportion (23.4%) were not followed post birth for the development of T2DM. Women with GDM are at high risk for developing T2DM and are

known to health services. Their follow up needs to be optimised with targeted diabetes prevention programmes developed to avoid progression to T2DM [32].

In this study, women who had no follow up were more likely to be non-white and to be nulliparous which may signpost possible targeted interventions including ensuring that information leaflets are available in different languages and formats.

The recently published NHS 10 year plan has highlighted maternity care, obesity and diabetes prevention as priorities to help improve health care inequalities and improve the population's health [33]. Opportunities to increase the awareness among women and clinicians of the risk of developing T2DM after GDM is required. Implementation of a national audit, as is already performed for pregnant women with Type1 and T2DM [34] to facilitate data acquisition to allow follow up and recall, reminder systems should be considered. These should take place alongside the development of effective evidence based preventive interventions which may include, counselling, advice on the importance of breast feeding, dietary and lifestyle changes and potentially pharmacological interventions.

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Table 1. Diagnostic criteria for GDM using the 75g oral glucose tolerance test.

	WHO 2013	IADPSG	NICE 2015
Fasting plasma glucose	5.1 -6.9 mmol/l	≥ 5.1 mmol/l	≥ 5.6 mmol/l
1 hour plasma glucose	≥ 10.0 mmol/l	≥ 10.0 mmol	
2 hour plasma glucose	8.5-11.0 mmol/l	≥ 8.5 mmol/l	≥ 7.8 mmol/l

Table 2. Gestational weight gain guidelines IOM 2009 [12]

Pre-pregnancy BMI kg/m²	Total weight gain (kg)
<18.5	12.5-18
18.5-24.9	11.5-16
25.0-29.9	7-11.5
≥ 30	5-9

Table 3. Characteristics of women with GDM.

Characteristic	Total sample	Women with T2DM	Women without T2DM	p value
Population *n* (%)	154	26 (16.9)	128 (83.1)	
Age (years)				0.422
Mean	32.4 (5.42)	31.2 (6.37)	32.66 (5.31)	
Body mass index (kg/m²)				
Mean	30.5 (7.30)	31.9 (9.06)	30.3 (6.93)	0.344
Missing	13			
BMI **category**				
Normal	33 (21.4)	6 (23.1)	27 (21.1)	
Overweight	30 (19.5)	4 (15.4)	26 (20.3)	0.866
Obese	78 (50.6)	13 (50)	65 (50.8)	
Missing	13 (8.4)	3 (11.5)	10 (7.8)	
Ethnicity recorded				
White	108 (70.1)	19 (73.1)	89 (69.5)	
Asian	22 (14.3)	4 (15.4)	18 (14.1)	0.903
Black	15 (9.7)	2 (7.7)	13 (10.2)	
Chinese	4 (2.6)	0 (0)	4 (3.1)	
Other	5 (3.2)	1 (3.8)	4 (3.1)	
Parity				
Primiparous	40 (26)	12 (46.2)	28 (21.9)	**0.01**
Multiparous	114 (74)	14 (53.8)	100 (78.1)	
Excessive GWG				
Yes	45 (29.2)	7 (27)	38 (29.7)	0.828
No	94 (61.1)	16 (61.5)	78 (60.9)	
Missing value	15 (9.7)	3 (11.5)	12 (9.4)	
Follow-up in years				
Mean	3.33 (2.55)	3.92 (2.12)	3.21 (2.63)	**0.002**
Median (range)	3.5 (0-8)	3 (1-8)	4 (0-8)	

Values are *n* (percent) unless otherwise stated.

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