



# **Postpartum Glucose Testing and Prevalence of Glucose Dysregulation after Gestational Diabetes Mellitus**

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## **Authors' contributions**

*This work was carried out in collaboration between all authors. Author PPSC designed the study, performed the statistical analysis and wrote the first and final draft of the manuscript. Author FCCT managed the data collection and analyses of the study. Authors LKT and AWES reviewed and critiqued the manuscript. All authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/BJMMR/2017/33465

Editor(s):

(1) Kate S. Collison, Department of Cell Biology, King Faisal Specialist Hospital & Research Centre, Saudi Arabia.

Reviewers:

(1) John Osaigbovoh Imaralu, Babcock University, Nigeria.

(2) V. Mohan, Madras Diabetes Research Foundation, India.

Complete Peer review History: <http://www.sciencedomain.org/review-history/19204>

**Original Research Article**

**Received 17<sup>th</sup> April 2017**

**Accepted 21<sup>st</sup> May 2017**

**Published 26<sup>th</sup> May 2017**

## **ABSTRACT**

**Aims:** To examine the prevalence of postpartum glucose testing in women with gestational diabetes mellitus (GDM), assess factors associated with return for testing and report the prevalence of glucose dysregulation in the postpartum period.

**Study Design:** Retrospective cohort study.

**Place and Duration of Study:** Joint Gestational Diabetes and Obstetrics Clinic in Singapore General Hospital, Singapore between 1 January 2013 and 31 December 2014.

**Methodology:** This study involved 307 women diagnosed with GDM. The result of the postpartum oral glucose tolerance test (ppOGTT) done between 6 weeks to 1 year post-delivery was reported. Patients were classified into normal, impaired fasting glucose (IFG) and/or impaired glucose

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tolerance (IGT) and diabetes.

**Results:** One hundred and ninety-one patients (62.2%) returned for ppOGTT within the 1 year period. The majority of them (93.2%, n=178) had their ppOGTT done within the first 12 weeks of delivery. Malay and Indian patients were less likely to return for ppOGTT compared to Chinese patients. Normal glucose tolerance was seen in 81.7% of patients, 16.2% had pre-diabetes (IFG and/or IGT), and 2.1% were diagnosed with diabetes.

**Conclusion:** The uptake of ppOGTT in Singapore is suboptimal, as with the trend reported worldwide. Further studies should be carried out to delineate characteristics of women who are least likely to return for ppOGTT. Thereafter, strategies can be formulated to encourage the uptake of ppOGTT by this target group of patients.

*Keywords: Gestational diabetes mellitus; glucose dysregulation; postpartum glucose testing.*

## 1. INTRODUCTION

Globally, we are observing an increasing frequency of gestational diabetes mellitus (GDM). This can be attributed to rising maternal age [1] as well as increasingly sedentary lifestyles, the latter also contributing to the epidemic of diabetes mellitus and obesity [2]. The International Diabetes Federation estimates that 16.2% of live births to women in 2015 had some form of hyperglycaemia in pregnancy, with an estimated 85.1% of this due to gestational diabetes [3].

The early identification of women with GDM allows for timely intervention and monitoring. While the National Institute for Health and Clinical Excellence (NICE) [4] in the United Kingdom recommends screening only in pregnant women at high risk for developing GDM, the United States practises universal screening of all pregnant women. Singapore, which previously used a targeted approach to screen high-risk patients, is now examining universal screening for GDM. This is based on a local study showing that universal screening detected significantly more cases [5] and is cost effective in reducing the complications of GDM [6].

GDM increases the risk for several adverse maternal and foetal outcomes. To the mother, these risks include pre-eclampsia, gestational hypertension and need for Caesarean section, while to the infant, there is a higher rate of macrosomia, birth injury, respiratory distress syndrome, hyperbilirubinaemia and neonatal care unit admissions [7]. Furthermore, women who have had GDM are at high risk for future development of impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and overt diabetes [8-10]. A meta-analysis of 675,455 women showed that the risk of developing type 2

diabetes mellitus (T2DM) is at least seven-fold increased in those with GDM compared to those with a normoglycaemic pregnancy [11]. The conversion rate from GDM to T2DM has been shown to be as high as 70% [12] with this rate largely dependent on factors such as length of follow up, ethnicity and diagnostic tests used. Asian women are particularly vulnerable; Indian women having an 11-fold increased risk of developing glucose intolerance in pregnancy compared to Caucasian women [13]. It is recommended that women with GDM be screened for persistent hyperglycaemia at 4 to 12 weeks postpartum using non-pregnancy criteria and every 1 to 3 years thereafter depending on other risk factors [14]. This should be done using a 75 g, 2-hour oral glucose tolerance test (OGTT).

The aim our study is to examine the prevalence of postpartum glucose testing in a racially diverse sample of women in Singapore and possible factors associated with returning for the test. Additionally, we also report the prevalence pre-diabetes (IFG and/or IGT) and T2DM in the postpartum period.

## 2. METHODOLOGY

### 2.1 Identification of Women with GDM

This was a retrospective cohort study involving women who were diagnosed with GDM between 1 January 2013 through 31 December 2014 and seen in the Joint Gestational Diabetes and Obstetrics Clinic in Singapore General Hospital (SGH), Singapore. SGH is a tertiary hospital with an annual number of deliveries of between 1800 and 2000.

A 75 g oral glucose tolerance test was performed in those deemed to be at high risk for GDM.

These included patients who fulfilled any of these criteria:

- (1) First degree relative with diabetes mellitus
- (2) High body mass index ( $BMI \geq 25 \text{ kg/m}^2$ )
- (3) Previous history of GDM or babies weighing  $>4 \text{ kg}$
- (4) Glycosuria (defined as urine dipstick showing urine glucose +1 or more)

Most of our patients were screened between 24–28 weeks gestation. This coincides with the onset of maternal insulin resistance, which begins in the second trimester and peaks in the third trimester. In women where glycosuria was detected earlier, the screening for GDM was offered before 24 weeks.

We adopted the 1999 World Health Organization (WHO) criteria for definition of GDM:  $\geq 7.0 \text{ mmol/L}$  for fasting glucose and/or  $\geq 7.8 \text{ mmol/L}$  for 2-hour after a 75 g oral glucose load.

## 2.2 Diabetes Care during Pregnancy

All patients diagnosed with GDM received counselling regarding their diagnosis from a healthcare nurse and also saw the hospital dietician who advised them on dietary modification. Advice was provided both verbally and in writing. They were also given instructions to monitor their home blood glucose readings pre- and post-meals and at bedtime. Patients were asked to report their home blood glucose readings during their medical appointments as well as via email in between clinic visits. Depending on the glucose readings, they were advised to either continue with dietary changes or commence on oral glucose-lowering therapy or insulin treatment at the discretion of the endocrinologist. The patients subsequently delivered their babies at SGH. Upon discharge from the hospital, they were given an appointment to return at 6 weeks postpartum for an OGTT, as well as to see their obstetrician for routine postpartum follow-up.

## 2.3 Postpartum Oral Glucose Tolerance Test (ppOGTT)

Postpartum screening was defined as performance of a 75 g 2-hour OGTT, after a 12 hour overnight fasting, at least 6 weeks after and within 1 year of delivery. Those who only had fasting plasma glucose done were excluded from our study. Patients were classified into normal, pre-diabetes, and diabetes. The pre-diabetes

category included patients with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). The former is defined by fasting glucose  $\geq 6.1 \text{ mmol/L}$  and the latter a 2-hour glucose of  $\geq 7.8 \text{ mmol/L}$  and  $< 11.1 \text{ mmol/L}$ . Diabetes was diagnosed by either fasting glucose  $\geq 7.0 \text{ mmol/L}$  or a 2-hour value of  $\geq 11.1 \text{ mmol/L}$ .

Time to the OGTT after delivery was calculated by determining the number of days from infant birth to the first testing date. This was further categorized into those who had the ppOGTT within 12 weeks and from 12 weeks up to 12 months. Patients who had their ppOGTT carried out after 12 months were excluded from this study.

## 2.4 Data Collection and Statistical Analysis

Information on maternal clinical, antenatal, delivery and postpartum glucose testing results were obtained from the patients' medical notes. We examined the demographic characteristics and the relation to ppOGTT (yes/no). Associations between the categorical variables and whether the patient returned for postpartum glucose testing were done using the chi-square test. Differences with  $P < .05$  were regarded as being statistically significant. For those who returned for ppOGTT, we determined the association between participation in this test and patient demographic factors using the multivariable logistic regression model. Result for each characteristic was presented as odds ratio (ORs) with 95% CI. All data analysis was done using the statistical package SPSS 22.0 (SPSS, Chicago, IL, USA).

## 3. RESULTS

A total of 358 patients with GDM were identified. Fifty-one patients were lost to follow-up due to transfer of care to a physician in a different hospital or country. The remaining 307 patients subsequently delivered their babies at SGH. The baseline characteristics of the 307 patients are shown in Table 1. The women included in our study consisted of 119 (38.8%) Chinese, 105 (34.2%) Malays, 60 (19.5%) Indians, and 23 (7.5%) from other ethnicities. The mean age was  $33.1 \pm 4.6$  years and mean body mass index (BMI)  $26.4 \pm 5.3 \text{ kg/m}^2$ . The mean gestational age at booking was  $12.1 \pm 5.7$  weeks.

In Table 2 we describe the characteristics of those who did and did not return for ppOGTT. The overall return rate for ppOGTT was 62.2%.

In the majority of patients, diet therapy alone was sufficient to adequately maintain their glucose targets. Treatment with either oral agents or insulin was required in 11.4% of patients.

In a multivariable logistic regression model shown in Table 3, we reported the demographic characteristics that were associated with returning for postpartum OGTT.

Table 4 shows the time between delivery date and returning for ppOGTT, as well as results of the postpartum glucose testing based on the different ethnicities. Of the patients who returned for ppOGTT, 156 (81.7%) were found to have normal glucose tolerance, while 31 (16.2%) had pre-diabetes (IFG and/or IGT), and 4 (2.1%) were diagnosed with diabetes.

**Table 1. Baseline characteristics of all patients with GDM**

	Total (n=307)				P
	Chinese (n=119)	Malay (n=105)	Indian (n=60)	Others (n=23)	
Age	34.2 ± 4.5	32.7 ± 4.5	32.1 ± 4.9	32.6 ± 4.6	.06
BMI	25.6 ± 5.0	26.3 ± 5.1	28.7 ± 6.1	25.5 ± 3.8	.61
Parity	0.7±0.9	0.9±1.0	1.4±1.4	1.1±0.8	.07
Gestational age at presentation	12.1 ± 6.1	11.1 ± 4.5	13.8 ± 6.7	10.9 ± 5.0	.49
Family history of DM	65 (54.6%)	66 (62.9%)	39 (65%)	13 (56.5%)	.98
History of GDM	18 (15.1%)	19 (18.1%)	9 (15%)	3 (13%)	.53
Average HbA1c in 2 <sup>nd</sup> trimester	5.1 ± 0.4	5.3 ± 0.5	5.5 ± 0.9	5.1 ± 0.6	.37
Average HbA1c in 3 <sup>rd</sup> trimester	5.2 ± 0.3	5.3 ± 0.6	5.6 ± 0.7	5.3 ± 0.5	.61

**Table 2. Characteristics of women who attended and did not attend postpartum glucose screening**

Characteristics	No postpartum glucose screening (n=116)	Postpartum glucose screening (n=191)	P
<b>Race</b>			.001
Chinese	28 (24.1%)	91 (47.6%)	
Malay	48 (41.4%)	57 (29.9%)	
Indian	30 (25.9%)	30 (15.7%)	
Other ethnicities	10 (8.6%)	13 (6.8%)	
<b>Age</b>			.14
≤30	41 (35.3%)	49 (25.6%)	
31-34	37 (31.9%)	62 (32.5%)	
≥35	38 (32.8%)	80 (41.9%)	
<b>BMI</b>			.63
≤25.0	48 (41.4%)	89 (46.6%)	
25.1-30.0	40 (34.5%)	66 (34.6%)	
30.1-35.0	19 (16.4%)	22 (11.5%)	
≥35.1	9 (7.7%)	14 (7.3%)	
<b>Parity</b>			.05
0	41 (35.3%)	81 (42.4%)	
1	38 (32.8%)	73 (38.2%)	
≥2	37 (31.9%)	37 (19.4%)	
<b>Family history of DM</b>			.84
No	46 (39.7%)	78 (40.8%)	
Yes	70 (60.3%)	113 (59.2%)	
<b>Treatment</b>			.51
Diet only	102 (87.9%)	170 (89.0%)	
Oral agents	8 (6.9%)	8 (4.2%)	
Insulin (+/- oral agents)	6 (5.2%)	13 (6.8%)	
<b>Mode of delivery</b>			.39
Vaginal delivery	64 (55.2%)	115 (60.2%)	
Caesarean section	52 (44.8%)	76 (39.8%)	

**Table 3. Multivariable logistic regression model predicting postpartum glucose testing screening among women with GDM**

Characteristics	Odds ratio (95% CI)	P
<b>Race</b>		
Chinese	1.00	
Malay	0.473 (0.242-0.925)	.03
Indian	0.353 (0.172-0.727)	.005
Others ethnicities	0.441 (0.170-1.143)	.09
<b>Age</b>		
≤30	1.00	
31-34	1.197 (0.629-2.280)	.58
≥35	1.519 (0.769-3.002)	.23
<b>BMI</b>		
≤25.0	1.00	
25.1-30.0	1.047 (0.598-1.835)	.87
30.1-35.0	0.889 (0.415-1.905)	.76
≥35.1	1.172 (0.436-3.152)	.75
<b>Parity</b>		
0	1.00	
1	0.935 (0.514-1.701)	.83
≥2	0.526 (0.266-1.038)	.06
<b>Family history of DM</b>		
No	1.00	
Yes	1.050 (0.634-1.739)	.85
<b>Treatment</b>		
Diet only	1.00	
Oral agents	0.538 (0.185-1.564)	.26
Insulin (+/- oral agents)	1.371 (0.483-3.893)	.55
<b>Mode of delivery</b>		
Vaginal delivery	1.00	
Caesarean section	0.823 (0.498-1.361)	.45

**Table 4. Time taken to return for and result of ppOGTT screening**

	Total (n=191)			
	Chinese (n=91)	Malay (n=57)	Indian (n=30)	Others (n=13)
<b>Time between delivery date and ppOGTT</b>				
<12 weeks	83	54	29	11
12 weeks to 12 months	8	3	1	2
<b>Glucose tolerance status</b>				
Normal	71	48	27	10
IFG	1	1	1	0
IGT	16	5	2	3
IFG and IGT	1	1	0	0
T2DM	2	2	0	0

#### 4. DISCUSSION

A significant proportion of women with GDM will go on to have persistently abnormal glucose levels post-delivery. In fact, the highest risk for the development of T2DM lies in those with a previous history of GDM [15]. To the mother, not only does GDM portend an increased risk for the development of T2DM, it is also a harbinger of other chronic health-related

conditions such as metabolic syndrome [16] and cardiovascular disease [17,18]. Long term negative effects have also been observed in the offspring. The abnormal intrauterine metabolic environment of a diabetic pregnancy negatively affects the neurodevelopmental outcome [19] and increases the risk of post natal metabolic complications such as abnormal glucose tolerance [20], obesity and metabolic syndrome [21].

The diagnosis of GDM offers an opportune time to screen and intervene in a high-risk population. Education, lifestyle modifications and pharmacotherapy in the postpartum period have been successful in reducing the prevalence of T2DM [22]. However, despite the recommendation for close follow-up after delivery, the uptake of ppOGTT across the world continues to be less than ideal [23-27].

The return rate for ppOGTT in our cohort was 62.2%, which is above the average reported in most studies. In a study conducted in another South East Asian country, the reported ppOGTT rate was 81.9% [28]. However, this was based on response rates collected via short message system (SMS) from patients, rather than data obtained from actual follow-up appointments. A study conducted in Canada [29] showed that postal reminders improved the attendance rate for ppOGTT, whereas a study using SMS reminders failed to show a similar outcome [30]. In a more recent study conducted in India, an impressive rate of 95.8% was achieved [31]. This project was undertaken as a joint exercise involving the government, the International Diabetes Federation and a philanthropic foundation and the replication of this result in day-to-day clinical care may be rather challenging.

In the multivariable logistic regression model, Malay and Indian patients were observed to be less likely to return for ppOGTT, compared with Chinese patients. This is in keeping with findings from other local studies showing increased odds of defaulting appointments in patients from these racial groups [32,33]. While we do not yet have the answers to explain this observation, this finding is of utmost significance. Singapore is the microcosm of Asia and provides a model on which we can forecast the burden of diabetes in Asia. The population of Singapore is made up of Chinese, Malays and Indians, and together these 3 ethnic groups account for two thirds of the world's population. Both the incidence and prevalence of T2DM is projected to rise markedly over the period of 1990 to 2050 for all three demographic groups, with the rate being steeper for the Malays and Indians. Given the large overlap of the risk factors for GDM and T2DM, we can assume the same trajectory for GDM. Of greater concern is the observation that Malay and Indian patients with diabetes have a risk profile roughly the same as a Chinese 10 years their senior [34]. Thus, it is paramount that efforts

are stepped up to ensure that these high risk patients return for ppOGTT and receive the necessary medical input to reduce their chances of developing long-term glucose dysregulation.

In our study, having 2 or more previous births almost reached statistical significance for predicting the failure to return for postpartum screening. Other studies have shown that the number of living children negatively predicted the likelihood of a woman returning for ppOGTT [27,35]. The postpartum period can be an extremely busy and challenging time for a mother, and more often than not, the need to care for young children takes precedence over her own health. Another possible factor is that of childcare availability. The OGTT is a time consuming process and mothers with difficulty fitting testing around their work and caregiving schedules may be less inclined to adhere to the appointment schedule.

There was a lack of statistical significance in the other variables studied such as age, BMI, family history of diabetes, type of treatment and mode of delivery in predicting the likelihood of returning for ppOGTT. Many reasons have been cited for the poor response rates, and these include perceptions that their diabetes would resolve after delivery of the baby, interpretation that the lack of reminder to reschedule missed appointments by their healthcare provider as indicators that they are at low risk of developing diabetes, as well as unpleasantness of the OGTT [28,36].

The majority of our patients (93.2%) returned for OGTT within 12 weeks of delivery. Of this, 16.2% was pre-diabetic, and 2.1% fulfilled the diagnostic criteria for T2DM. The rate of postpartum dysglycaemia seen in this study is comparable to that observed in other studies [27,37]. We excluded patients who only had fasting plasma glucose done as this has been shown to miss up to 40% of patients with T2DM and fail to identify those with IGT [38]. Assuming that approximately 20% of those tested had some form of dysglycaemia, the observation that 40% of patients with GDM did not return for ppOGTT will translate to about 23 cases of dysglycaemia being missed over a 2 year period. This is likely to be an underestimation, given the fact that high-risk screening (as adopted in our study) only detected half of GDM cases that would have otherwise been diagnosed via universal screening [5].

The importance of postpartum glucose testing cannot be over-emphasised. Missing the diagnosis of dysglycaemia in this group of patient can have very serious long term implications. Firstly, these women are of child bearing potential and may go on to have undiagnosed T2DM in their future pregnancies. Maternal hyperglycaemia at the time of conception and in the first trimester can result in diabetic embropathy, giving rise to spontaneous abortions and major congenital birth defects [39]. Secondly, the early identification of women with postpartum dysglycaemia enables the timely intervention to prevent progression to overt diabetes. This was elegantly demonstrated in The Diabetes Prevention study where both lifestyle intervention and medical therapy with metformin delayed the onset of T2DM in women with previous GDM [22].

#### 4.1 Study Strength and Limitation

Our study was limited by our inability to obtain information on educational and income status, both of which have been shown to influence the uptake of postpartum glucose screening among women with history of GDM [27,35].

The strength of our study includes the fact that this is the first study based on a multiracial population in South East Asia with data on postpartum glucose testing result, enabling us to determine the rate of glucose dysregulation after delivery.

#### 5. CONCLUSION

Our study highlights the fact that the uptake for postpartum glucose testing continues to be suboptimal. Postpartum glucose testing is a vital step that should be taken so that clinical intervention can be made to reduce the recurrence of GDM in subsequent pregnancies and the development of non-gestational glucose dysregulation. The population of pregnant women with GDM will continue to grow in the years to come. Further studies involving a larger number of patients in our population are needed so as to delineate characteristics of women who are least likely to return for a ppOGTT, and understand their health-seeking behaviours and attitudes. The use of telephone, SMS and email to remind women to obtain postpartum glucose testing are some of the avenues that can be explored. This way, we will hopefully be able to tailor targeted interventions aimed at those with the highest risk of attrition.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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