

Adherence to postpartum screening in women diagnosed with gestational diabetes: a retrospective single-centre experience in Switzerland

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Summary

STUDY AIMS: A history of gestational diabetes mellitus is a known risk factor for developing type 2 diabetes in the future. Therefore, screening for persistent dysglycaemia in the postpartum period is of utmost importance. However, follow-up rates tend to be low. The aim of this study was to investigate postpartum screening adherence at a tertiary care centre and to identify factors contributing to persistent dysglycaemia.

METHODS: A cohort of women with gestational diabetes mellitus diagnosed between 2015 and 2018 at the department of Obstetrics and Gynaecology, University Hospital Bern, Switzerland, was retrospectively studied. Ethnicity, parity, pre-pregnancy BMI, family history of diabetes mellitus, first trimester glycosylated haemoglobin (HbA1c), 75 g oral glucose tolerance test during pregnancy and in the postpartum period were analysed. Postpartum dysglycaemia was defined as overt diabetes (fasting plasma glucose ≥ 7.0 mmol/l and/or 2 hours plasma glucose ≥ 11.1 mmol/l for the 75 g oral glucose tolerance test), impaired glucose tolerance (2 hours plasma glucose 7.8–11.0 mmol/l) or impaired fasting glucose (plasma glucose 5.6–6.9 mmol/l). Parametric and non-parametric tests as well as multivariate regression were used. ROC analyses were performed to assess the prognostic accuracy of HbA1c and oral glucose tolerance test results at predicting postpartum dysglycaemia.

RESULTS: We included 489 women with gestational diabetes mellitus in our study. Of these, 217 (44.4%) returned for postpartum testing and 59/217 (27.2%) had an abnormal oral glucose tolerance test. Ethnicity was found to be a factor in adherence to follow-up. Specifically, women of African origin showed a significantly higher compliance than Asian or Caucasian women (61.8% vs 47.8% vs 34.5%, respectively; $p = 0.04$). The multivariate analysis revealed that obesity (OR: 3.64, 95% CI: 1.41–9.37) and first trimester HbA1c $> 5.7\%$ (OR: 3.67, 95% CI: 1.28–10.52) are significantly associated with an increased risk of postpartum dysglycaemia.

CONCLUSION: Our study indicates that adherence to postpartum screening after gestational diabetes mellitus is low but in line with the existing experience. This is of particular concern as 1 of 4 women undergoing postpartum screening show some sort of disturbed glucose metabolism. In particular, women with higher first trimester HbA1c and/or obesity may warrant closer observation and motivation for testing as the risk for persistent metabolic disorders is increased.

Introduction

Gestational diabetes mellitus is a disorder of glucose metabolism that is usually first diagnosed in the second or third trimester of pregnancy and resolves after birth. A systematic and generalised screen for gestational diabetes mellitus after the 24th week of gestation is now a recognised standard of prenatal care as its treatment has been associated with a better pregnancy and perinatal outcome [1].

Additionally, this screening might also be an opportunity to improve the long-term health status of these women. Indeed, it has been recognised that adverse pregnancy outcomes might be associated with future systemic diseases. Preeclampsia is one of these pregnancy complications that has been strongly associated with future cardiovascular disorders [2]. Similarly, women with gestational diabetes mellitus are at increased risk of developing type 2 diabetes mellitus later in life [3]. This is of particular relevance as today's society is faced with a pandemic prevalence of obesity, an important additional risk factor for cardiovascular as well as metabolic diseases [4]. This trend is also of concern within the obstetric population [5].

According to the definition of gestational diabetes, a pre-existing dysglycaemia must be excluded after delivery [1]. This is similar to the definition of hypertensive complications during pregnancy. High blood pressure usually has to normalise at the latest 3 months after delivery [6]. Consequently, most international diabetes and obstetric societies as well as international organisations suggest searching for persistent diabetic disorders after delivery in women where pregnancy was complicated by gestational diabetes melli-

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tus [1, 7]. The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommends performing a postpartum 75 g oral glucose tolerance test [7]. The blood sugar cutoffs used to exclude or diagnose diabetes are those proposed for the non-pregnant population [1, 7]. Since 2011 the Swiss Society of Obstetrics and Gynaecology together with the Society of Endocrinology have recommended to use the same diagnostic criteria of gestational diabetes mellitus in Switzerland [8]. Accordingly, it is therefore proposed to offer an oral glucose tolerance test 4 to 8 weeks after delivery. However, international data shows low adherence to this postpartum testing modality [9–11].

The aims of this study were therefore to investigate adherence to postpartum oral glucose tolerance test screening at a tertiary care centre in Switzerland and to analyse the incidence of persistent dysglycaemia after delivery as well as to unravel its potential contributing factors.

Materials and methods

We included pregnant women who were diagnosed with gestational diabetes mellitus from 2015 to 2018 by a one-step standardised 75-g oral glucose tolerance test between 24 and 28 weeks of gestation as proposed by the International Association of the Diabetes and Pregnancy Study Groups and adopted by the Swiss Society of Obstetrics and Gynaecology in 2011 [7, 8]. These women are a subset of patients who were enrolled in a prospective study investigating the role of glycosylated haemoglobin (HbA1c) and maternal characteristics in predicting gestational diabetes mellitus [12]. We excluded patients who were not screened within the recommended timeframe and for whom we did not have complete information on the oral glucose tolerance test values. Venous blood samples were collected at 0, 1 and 2 hours after the glucose load. Women with preexisting diabetes mellitus or a first trimester HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol) were excluded from the study. In accordance with current guidelines, the diagnosis of gestational diabetes mellitus was made when any of the following criteria was met on the 75-g oral glucose tolerance test: plasma glucose ≥ 5.1 mmol/l in the fasting state and/or ≥ 10.0 mmol/l at 1 hour and/or ≥ 8.5 mmol/l at 2 hours [7, 8, 13].

The following information was assessed from our electronic patient database: age, ethnicity, parity, pre-pregnancy body mass index (BMI), family history of diabetes mellitus (first-degree relatives), history of gestational diabetes mellitus, first trimester HbA1c [12], gestational age at oral glucose tolerance test and plasma glucose values at fasting, at 1 hour and at 2 hours, management of gestational diabetes mellitus during pregnancy (lifestyle and/or insulin treatment), gestational age at delivery, mode of delivery, birthweight, incidence of neonatal hypoglycaemia (blood glucose ≤ 2.5 mmol/l), values of postpartum oral glucose tolerance test (fasting and at 2 hours) and time point of postpartum oral glucose tolerance test screen.

Fasting plasma glucose levels in the range 5.6–6.9 mmol/l were considered as impaired fasting glucose and ≥ 7.0 mmol/l as diabetes. At 2 hours, a value in the range 7.8–11.0 mmol/l indicated impaired glucose tolerance and ≥ 11.1 mmol/l confirmed the diagnosis of diabetes [1].

The primary goal of this study was to investigate the percentage of women with gestational diabetes mellitus not adhering to the recommended postpartum follow-up. Secondly we wanted to describe the differences between those who came to postpartum testing and those who did not. We further analysed the percentage of persistent dysglycaemia and possible prenatal risk factors.

Statistical analyses were performed using GraphPad Prism version 8.2.1 and SPSS version 26 for Windows. Univariate and multivariate logistic regression analyses of factors associated with an abnormal postpartum oral glucose tolerance test result (impaired fasting glucose / impaired glucose tolerance / diabetes) at 1–3 months after delivery were performed. Student's t-test was used for the comparisons of continuous variables (age, BMI, first trimester HbA1c, gestational age) in the follow-up and no follow-up group.

Proportions were analysed using the chi-square test or Fisher's exact test as appropriate. A p-value of <0.05 was considered significant.

The study was approved by the institutional ethics committee of the canton of Bern (Ethics Committee of the Canton of Bern, Switzerland, Basec-Nr.: 2016-00415). General consent was obtained from the patients.

Results

During the study period, we were able to include 489 women fulfilling the diagnostic criteria for gestational diabetes mellitus. The clinical and demographic characteristics of the study population are shown in table 1. Of these women, 217 (44.4%) underwent postpartum testing while the remaining 272 (55.6%) were lost to follow-up. The only statistically significant differences between women with follow-up and those without were age and ethnicity (table 2). Specifically, African women returned significantly more often for postpartum oral glucose tolerance test screening than Caucasian women. The percentages of women with a postpartum oral glucose tolerance test were 107/285 (34.5%), 55/115 (47.8%) and 55/89 (61.8%) for Caucasian, Asian and African women, respectively. As regards the age-dependent effect, older women adhered better to the proposed postpartum screening than younger women. This was particularly true for Caucasian women (with oral glucose tolerance test 34.1 years vs without oral glucose tolerance test 32.2 years old, $p = 0.007$), while no age difference was observed in Asian and African women (with oral glucose tolerance test 31.8 years vs without oral glucose tolerance test 30.7 years, $p = 0.16$). The median [range] interval between the delivery and the postpartum oral glucose tolerance test was 55 [49–90] days. In 71.9% of the cases, follow-up was performed within 12 weeks of delivery (Caucasian 71.0%, African 81.8%, Asian 63.6%), and in 12.4% within 6 weeks postpartum.

Of the women who returned for postpartum screening, an abnormal oral glucose tolerance test result was detected in 59/217 (27.2%): 52/217 (24%) had dysglycaemia (impaired fasting glucose and/or impaired glucose tolerance) and 7/217 (3.2%) women were diagnosed with overt diabetes mellitus.

To analyse factors associated with an increased risk for an abnormal postpartum oral glucose tolerance test, we performed univariate and multivariate analyses including age,

obesity, family history of type 2 diabetes, personal history of gestational diabetes mellitus and first trimester HbA1c in the prediabetes range ($\geq 5.7\%$ and $< 6.5\%$). All patients lacking a complete dataset (first trimester HbA1c, oral glucose tolerance test values obtained during and after pregnancy or BMI) were excluded from this analysis ($n = 132$). A postpartum abnormal oral glucose tolerance test was associated with pre-pregnancy obesity and first trimester HbA1c $\geq 5.7\%$ (table 3). Additionally, to investigate the diagnostic performance in predicting postpartum dysglycaemia, first trimester HbA1c and glucose levels obtained from the oral glucose tolerance test during pregnancy were compared between women with and without persistent dysglycaemia after delivery. All values (HbA1c, fasting plasma glucose, plasma glucose at 1 hour and 2 hours after the oral glucose tolerance test) were significantly different between the two groups, regardless of the aforementioned HbA1c cutoff value of $\geq 5.7\%$ used in the regression analyses (table 4).

Discussion

Our results show that not even half of our study population with gestational diabetes mellitus returned for postpartum screening. This contrasts with the number of women who follow the screening recommendations during pregnancy. Indeed, since the introduction of the IADPSG criteria for screening for gestational diabetes mellitus in Switzerland in 2011, the prevalence has increased 3-fold [8, 14]. To compare our results on adherence to postpartum testing with those of others, we performed a PubMed search on the existing literature with similar screening strategies during that period. We found twelve studies, in which the mean postpartum follow-up rate of women with gestational diabetes mellitus was 49.5%, ranging individually from 17.0% to 92.9% [10, 11, 15–24]. Our percentage of adherence to the postpartum oral glucose tolerance test screening is in line with that found in this short review of the literature. Quaresima et al. reported that reasons for non-compliance were misunderstood importance, oversight,

Table 1:

Clinical and demographic characteristics of the study population ($n = 489$). The results are presented as mean $\pm$ SD, or median (range), or n (%).

Clinical characteristics		Results
Age at delivery, in years		32.2 $\pm$ 5.9
Ethnicity, n (%)	Caucasian	285 (58.3)
	Asian	115 (23.5)
	African	89 (18.2)
Parity		2 (1–3)
Parity, n (%)	Nulliparous	133 (27.2)
	Second pregnancy	142 (29.0)
	>2 pregnancies	214 (43.8)
History of gestational diabetes mellitus, n (%)*		64 (13.1)
Family history of diabetes, n (%)		94 (19.2)
Pre-pregnancy BMI, in kg/m^2		26.9 $\pm$ 5.9
Pre-pregnancy BMI ≥ 30 , n (%)		103 (21.1)
First trimester HbA1c, in %		5.5 $\pm$ 0.9
Insulin treatment, n (%)		236 (48.3)
Gestational age at delivery in weeks		38.6 $\pm$ 1.6
Mode of delivery, n (%)	Spontaneous	228 (46.6)
	Vaginal operative	52 (10.6)
	Caesarean section	209 (42.7)
Birth weight in g		3228 $\pm$ 305
Birth weight ≥ 4 kg, n (%)		28 (5.9)
Neonatal hypoglycaemia, n (%)		20 (4.2)

BMI: body mass index; HbA1c: glycosylated haemoglobin.

* 18% ≥ 1 previous pregnancy

Table 2:

Comparison of women with vs without follow-up oral glucose tolerance test screening in the postpartum period. The results are presented as mean $\pm$ SD, or median (range), or n (%).

Characteristics	Follow-up ($n = 217$)	No follow-up ($n = 272$)	p-value
Age, in years	32.9 $\pm$ 6.3	31.7 $\pm$ 5.6	0.02
BMI, in kg/m^2	26.3 $\pm$ 5.9	26.2 $\pm$ 5.2	0.69
First trimester HbA1c, in %	5.2 $\pm$ 0.3	5.3 $\pm$ 0.3	0.48
Ethnicity			<0.0001
...Caucasian, n (%)	107 (34.5)	178 (65.5)	
...Asian, n (%)	55 (41.8)	60 (58.2)	
...African, n (%)	55 (61.8)	34 (38.2)	
Gestational age at delivery in weeks	38.7 $\pm$ 1.4	38.6 $\pm$ 1.8	0.64
Nulliparity, n (%)	81 (29.8)	52 (23.9)	0.15
Insulin treatment, n (%)	106 (48.8)	130 (47.8)	0.86
Caesarean section rate, n (%)	92 (42.4)	117 (43.0)	0.93

BMI: body mass index; HbA1c: glycosylated haemoglobin.

newborn care, non-availability of test reservation in the centre and – more concerning – discouragement by primary care physicians [24]. Postpartum proactive reminder systems may increase the uptake of testing for type 2 diabetes in women with previous gestational diabetes mellitus. However, studies using SMS reminders after delivery did not show a significant improvement in the rate of postpartum screening [25, 26]. One of the main criticisms reported by women was that the test was inconvenient and a shorter one would be preferable [27].

Surprisingly, our findings show that younger Caucasian women, in whom we would not expect communication problems, were the least likely to attend for postpartum screening. Although it is common knowledge that gestational diabetes mellitus poses a greater risk for type 2 diabetes in the future and despite the fact that non-compliance factors have already been elucidated and attempts made to overcome them, a tangible effect on the postpartum screening rate has not yet been seen.

In our ethnically diverse cohort, over one quarter of the women who returned for screening had abnormal test results. Conversely, this means that we are missing many young women and mothers who would benefit greatly from early diagnosis and treatment such as lifestyle modifications or medications as well as surveillance to reduce the harmful effects of a disturbed glucose homeostasis.

Our univariate and multivariate analyses revealed that first trimester HbA1c $\geq 5.7\%$ and obesity are each associated with an abnormal postpartum oral glucose tolerance test. By focusing and insisting on postpartum testing in at least these high-risk women, we could make a core contribution to the health of women and thus also of the family and society in general. Amylidi et al. have shown that first trimester HbA1c is of value in distinguishing pregnant women at risk of developing gestational diabetes and levels $\geq 6.0\%$ (42 mmol/mol) are predictive of gestational diabetes mellitus during pregnancy [12]. It has been stated that this information may be useful for counselling these women and providing appropriate advice on diet and

lifestyle modification early in pregnancy. Our results add additional support to first trimester gestational diabetes mellitus screening using HbA1c as it could also be of value in distinguishing those women at risk of persistent dysglycaemia. First trimester HbA1c as a screening tool for postpartum dysglycaemia in women with gestational diabetes mellitus during their pregnancy is – although statistically significant – not outstanding and not better than the plasma glucose values obtained from the third trimester oral glucose tolerance test. However, the feasibility is more convenient as it only requires one blood sample, does not need prior fasting, is less time- and resource-consuming, and could therefore easily be integrated into routine pregnancy care and post-delivery screening. In the Swiss guidelines, the use of HbA1c to exclude overt diabetes ($>6.5\%$) has been proposed as an alternative screening tool [8]. In our cohort of women with postpartum dysglycaemia, 11.9% (7/59) fulfilled the diagnostic criteria for overt diabetes while 88.1% (52/59) had prediabetes using the oral glucose tolerance test-based definitions. Further prospective studies are needed to evaluate the practicability and predictive value of a postpartum 75 g oral glucose tolerance test or HbA1c in screening not only for overt diabetes but also other forms of dysglycaemia. To increase adherence to this postpartum screening, the paediatrician could play a key role. Indeed, in Switzerland regular newborn screening is recommended at one week, and then at one, two, four, six, nine and twelve months of life [28]. As the child is often accompanied by its mother, the opportunities to remind the woman – or even for the paediatrician to perform the postpartum screening – could be an interesting option that should be further discussed. Furthermore, the motivational support by midwives could be of utmost importance in increasing screening adherence.

Our study has several strengths and limitations. The strengths lie in a uniform screening method according to current guidelines during and after pregnancy. Moreover, the fact that our cohort is extracted from another study [8] has given us the opportunity to investigate the role of

Table 3: Univariate and multivariate logistic regression analyses of factors associated with abnormal postpartum oral glucose tolerance test (impaired fasting glucose / impaired glucose tolerance / diabetes) at 1–3 months after delivery (n = 206). 283 patients did not perform the postpartum oral glucose tolerance test and therefore are not part of these analyses. Multivariate models were carried out for variables reporting a p-value ≤ 0.01 in the univariate analysis.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.03 (0.97–1.1)	0.206		
BMI ≥ 30 kg/m ² (Yes vs No)	3.98 (1.62–9.75)	0.002	3.64 (1.41–9.37)	0.007
Family history of diabetes (Yes vs No)	0.56 (0.22–1.42)	0.22		
History of gestational diabetes mellitus (Yes vs No)	3.07 (1.19–7.88)	0.01	1.97 (0.67–5.76)	0.21
First trimester HbA1c $\geq 5.7\%$ (Yes vs No)	4.91 (1.88–12.82)	0.001	3.67 (1.28–10.52)	0.01

Table 4: Comparison of first trimester HbA1c as well as fasting plasma glucose, 1 hour and 2 hours plasma glucose values from 75 g oral glucose tolerance test during pregnancy in women with vs without persistent dysglycaemia postpartum. The results are presented as mean $\pm$ SD, or median (range).

Characteristics	Dysglycaemia postpartum (n = 39)	No dysglycaemia postpartum (n = 95)	Area under the curve (95% CI)
First trimester HbA1c, in %	5.47 $\pm$ 0.40	5.27 $\pm$ 0.36	0.63 (0.53–0.74)
Fasting plasma glucose, in mmol/l	5.30 (4.39–9.10)	5.10 (4.10–8.16)	0.68 (0.59–0.77)
Plasma glucose at 1 hour after oral glucose tolerance test, in mmol/l	10.64 (6.93–17.19)	10.08 (4.10–13.90)	0.61 (0.52–0.71)
Plasma glucose at 2 hours after oral glucose tolerance test, in mmol/l	8.26 (4.83–16.10)	7.77 (4.43–12.5)	0.61 (0.50–0.71)

95% CI: 95% confidence interval; HbA1c: glycosylated haemoglobin.

first trimester glycosylated haemoglobin also after delivery. Furthermore, our study cohort consists of an ethnically broad spectrum, which gave us the possibility to also investigate ethnic differences. However, our study is not without limitations. Due to incomplete datasets, the analyses could not be performed on the whole cohort. In addition, we have no sound information on why the women did not return for postpartum testing. Furthermore, a selection bias is possible due to the fact that all women were seen at our tertiary care facility. Additionally, we had a high proportion of non-Caucasian women who adhered to postpartum screening. Women of Asian and African ethnicity have a higher incidence of disturbances of glucose metabolism. This could explain the relatively high number of dysglycaemia in postpartum screening in our study population.

In conclusion, a lot of work and multidisciplinary effort is still required to increase adherence to screening measures after gestational diabetes mellitus in the short as well as the long term. Our results may help to better identify women at risk of persistent postpartum dysglycaemia or even diabetes. Incorporating screening results already obtained during pregnancy and a more comprehensive education of these women and other healthcare providers, such as paediatricians and midwives, could help to curb the increasing burden of this metabolic disorder in our society.

Data sharing statement

Individual participant data that underlies the results reported in this article will be available from 9 months to 36 months following the publication of this article. The dataset generated or analysed during the current trial is available from the corresponding author on reasonable request.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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