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Repeated oral glucose tolerance tests in women at risk for gestational diabetes mellitus

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ABSTRACT

Objective: Pregnant women with a negative oral glucose tolerance test (OGTT) between 24–28 weeks as part of risk-based screening for gestational diabetes mellitus (GDM) may develop clinical signs or symptoms suggestive for GDM in the third trimester. We aimed to determine the additional yield of repeating an OGTT to detect missed GDM in this group and assess patient characteristics and indications associated with a positive second OGTT.

Study design: We conducted a retrospective cohort study of women with a negative OGTT between 24–28 weeks of pregnancy in two hospitals in the Netherlands. Patient characteristics, pregnancy outcomes, OGTT results and indications were compared between women with normal (non-GDM) and abnormal (GDM) results of the second OGTT, using the WHO 1999 criteria (fasting glucose ≥7.0 mmol/L or 2 -h post load ≥7.8 mmol/L). We used receiver operating characteristic (ROC) curve analysis to determine cut-offs for fasting and 2 -h glucose values of the index OGTT that were associated with a positive OGTT in the third trimester.

Results: Of 3147 women at risk for GDM, 183 underwent a second OGTT in the third trimester following their regular OGTT at 24–28 weeks. In 43 women (23.5%) GDM was diagnosed based on the second OGTT. A history of GDM was associated with subsequent GDM diagnosis, with an odds ratio of 2.6 (95% CI 1.0–6.3). Both fasting and 2 -h post load glucose values of the index OGTT were significantly higher in women with abnormal OGTT results later in pregnancy. Index OGTT glucose value cut-offs of 4.8 mmol/L (fasting) and 6.5 mmol/L (2 -h) had positive predictive values of 0.32 and 0.47 for a positive OGTT in the third trimester, and negative predictive values of 0.83 and 0.90, respectively. Fetal growth as a clinical symptom for GDM was the most frequent indication for repeating the OGTT, resulting in the diagnosis of GDM in 22.7% of women tested for this indication.

Conclusion: Repeating an OGTT after initial negative screening results in additional GDM diagnoses. In case of clinical signs, especially in women with additional risk factors such as a history of GDM or higher index OGTT glucose values, repeating an OGTT could be considered.

Introduction

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy, is one of the most common metabolic disorders complicating pregnancy [1]. Worldwide the prevalence of GDM ranges from 2 to 32%, varying greatly depending on the screening methods, the population tested and cut-offs used [2–4]. In the Netherlands approximately 5% of pregnant women develop GDM [5,6].

The incidence of GDM, most notably occurring in the second or third trimester, is rising and is increasingly contributing to perinatal complications such as macrosomia, shoulder dystocia, caesarean section and neonatal hypoglycemia [7–11]. Moreover, long term sequelae of gestational diabetes mellitus include progression to type 2 diabetes in mothers and obesity in their offspring [12–16]. Accurate and

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timely diagnosis allows for appropriate treatment, reducing these risks [17,18]. It is still unclear which screening- and testing methods or which criteria offer the best improvement of maternal and fetal health [19–21].

Clinical guidelines recommend screening for GDM in pregnancy, either universal or based on the presence of risk factors, such as obesity, a history of GDM and a family history of diabetes [22–24]. The oral glucose tolerance test (OGTT) is mostly used to diagnose GDM, performed at 24–28 weeks of gestation and in some cases also in the first trimester. However, other risk factors that are associated with the presence of GDM, such as suspected fetal macrosomia, polyhydramnios or glycosuria may develop or are first detected later in pregnancy [25–27]. Several guidelines recommend further testing to exclude undiagnosed GDM in the presence of signs suggestive for GDM [23,24]. Although these risk factors have been found to have a positive predictive value of up to 40–50% for GDM in unscreened women, the additional yield is of repeating the OGTT when clinical symptoms occur in women that already have been screened earlier in pregnancy is currently unknown [25].

The aim of this study was to determine to what extent repeating an OGTT in women with risk factors suggestive for GDM after initial negative screening between 24–28 weeks of pregnancy results in additional GDM diagnoses. Also we sought to determine patient characteristics and risk factors associated with a positive OGTT in the second place and subsequent GDM diagnosis later in pregnancy.

Materials and methods

For this retrospective cohort study all women undergoing multiple OGTTs to test for GDM during a single pregnancy were identified in the Haaglanden Medical Center Bronovo (2013) and University Medical Center Utrecht (2013–2015) using laboratory records. To ensure completeness and rightful inclusion laboratory data was cross-referenced with the obstetric patient files. The study was approved by the research ethics committee of Zuidwest Holland (reference number 18–101) and University Medical Center Utrecht (reference number 16–711/C).

In the Netherlands pregnant women are screened for GDM based in predefined risk factors: intake BMI >30 kg/m^2, family history of diabetes, previous GDM, history of macrosomia or unexplained stillbirth, polycystic ovarian syndrome (PCOS), and patients belonging to an ethnic group with presumed higher incidence of type 2 diabetes and/or GDM [24]. In women with one or more risk factors a 75-gram OGTT is performed between 24–28 weeks of pregnancy. In case of a history of GDM, an early extra OGTT test is advised at 16 weeks of gestation, which is then repeated between 24–28 weeks if negative. In women presenting with clinical signs suggestive for GDM, such as accelerated fetal growth, suspected macrosomia, polyhydramnios or symptoms such as rapid weight gain, polydipsia or excessive thirst, an OGTT is indicated at any time during pregnancy regardless of the presence of risk factors.

The OGTTs were performed by standardized protocol after overnight fasting, using venous samples. After the fasting glucose sample, a drink containing 75 g of glucose was ingested and the second venous sample was obtained after 2 h. The WHO 1999 criteria were used to diagnose GDM (venous fasting plasma glucose $\geq$7.0 mmol/L or 2 -h value $\geq$7.8 mmol/L). The diagnosis of GDM was made when one or more values exceeded these thresholds, after which women were referred to a dietician for medical nutritional therapy and received care from a multidisciplinary team, including an internal medicine specialist and gynecologist. In case of insufficient glycemic control by means of dietary adaptations insulin treatment was initiated.

In this cohort we selected women undergoing an OGTT between 24–28 weeks according to the Dutch screening protocol (OGTT1), followed by an additional OGTT in the same pregnancy (OGTT2). These were divided into two groups: women undergoing 2 OGTTs of which both tests yielded negative results (NEG-NEG, non-GDM) and women of which the index test was negative and the second indicative for GDM (NEG-POS, GDM).

For all patients, maternal characteristics, risk factors for GDM, pregnancy characteristics, ultrasound data and pregnancy outcomes were extracted from electronic patient files. Also healthcare provided indications for OGTT1 and OGTT2 were collected. In some cases more than 1 reason for the OGTT was given. Fetal growth as

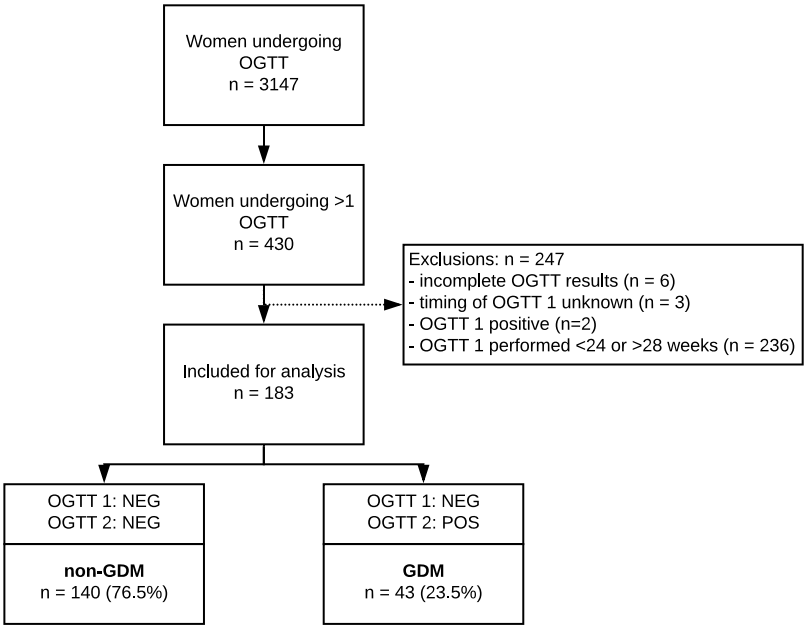

Fig. 1. Study flow-chart of OGTTs in pregnant women in the study period.
OGTT: oral glucose tolerance test, NEG: negative, POS: positive, GDM: gestational diabetes mellitus

an indication for the OGTT consisted of a clinical suspected macrosomia or accelerated fetal growth, either based on ultrasound measurements or physical examination. Dutch reference curves were used for the determination of FAC (fetal abdominal circumference) and EFW (estimated fetal weight) measurements by ultrasound and birth weight percentiles [28,29]. Birth weight percentiles are adjusted for parity, neonatal sex and gestational age. Polyhydramnios was defined as a single deepest pocket of amniotic fluid >8 cm or amniotic fluid index (AFI) $\geq 95^{th}$ centile.

Statistical analyses

Data is summarized as frequencies and percentages for categorical variables and as mean ± standard deviation or median with interquartile range for continuous variables. Differences between the groups were compared using the chi-square test and Fisher's exact test for categorical variables and a Student's *t*-test or Mann-Whitney U test for continuous variables, depending on distribution. Odds ratios (OR) and corresponding 95% confidence interval (95% CI) were calculated using logistic regression analysis. We furthermore used logistic regression analysis and receiver operating characteristic (ROC) plots to determine cut-offs for fasting and 2-h post load glucose values of OGTT1 that were associated with a positive OGTT2 [30]. The Youden index was used to determine the optimal cut-offs [31]. Corresponding 2 × 2 tables were used to calculate sensitivity, specificity, positive and negative predictive values (PPV/NPV) and likelihood ratios. Positive and negative likelihood ratios were used to calculate post-test probabilities for a positive second OGTT [32]. The level of significance was set at $p = <0.05$. Analyses were performed with SPSS for Windows version 25 (SPSS Inc., Chicago, IL, USA).

Results

In the study period a total of 3147 pregnant women were booked for an OGTT to test for GDM (Fig. 1). Of these, 430 women

Table 1
Maternal characteristics, risk factors and pregnancy outcomes for non-GDM (NEG-NEG) and GDM (NEG-POS) groups.

Characteristic	non-GDM (NEG-NEG) n = 140	GDM (NEG-POS) n = 43	p-value
Maternal age – years	33 (30–36)	35 (30–38)	0.242
Maternal age ≥35 years – n (%)	51 (36.4)	21 (51.2)	0.084
Maternal age ≥40 years – n (%)	14 (10.0)	6 (14.0)	0.467
BMI – kg/m^2	25.5 (22.6–32.0)	28.0 (24.5–32.0)	0.100
BMI >30 kg/m^2 – n (%)	45 (32.4)	15 (34.9)	0.760
Gravidity	2 (2–3)	3 (2–4)	0.039
Primiparous – n (%)	42 (30.0)	13 (30.2)	0.977
Ethnicity – Caucasian – n (%)	78 (55.7)	23 (53.5)	0.797
PCOS – n (%)	5 (3.6)	3 (7.0)	0.339
Conception – spontaneous – n (%)	123 (87.9)	36 (83.7)	0.482
Obstetric history*: n (%)			
Intrauterine fetal death	3 (3.8)	1 (4.0)	0.955
Macrosomia	33 (33.7)	11 (36.7)	0.763
GDM	18 (18.4)	11 (36.7)	0.036
Family history DM – n (%)	44 (31.4)	17 (39.5)	0.324
Number of risk factors: n (%)			
1	53 (37.9)	17 (39.5)	0.843
≥2	61 (43.6)	24 (55.8)	0.159
OGTT 1:			
Gestational age – weeks	25.6 (24.6–26.8)	25.3 (24.6–26.4)	0.631
Fasting plasma glucose – mmol/L	4.8 (4.6–5.1)	4.9 (4.7–5.2)	0.028
2-hour glucose – mmol/L	5.7 (4.9–6.6)	7.1 (6.3–7.5)	<0.001
OGTT 2:			
Gestational age – weeks	33.3 (31.8–35.0)	33.1 (35.1)	0.966
Fasting plasma glucose – mmol/L	4.8 (4.5–5.1)	5.0 (4.7–5.3)	0.009
2-hour glucose – mmol/L	6.4 (5.6–7.0)	8.4 (8.0–9.3)	<0.001
Ultrasound: n (%)			
FAC >90th percentile	113 (80.7)	33 (76.7)	0.571
EFW >90th percentile	82 (58.6)	21 (48.8)	0.260
Polyhydramnios	14 (10.0)	3 (7.0)	0.766
Gestational age at birth - weeks	39.9 (39.0–40.7)	39.3 (38.7–40.1)	0.022
Preterm birth (<37 weeks)	5 (3.7)	1 (2.3)	1.000
Onset of labour: n (%)			
Spontaneous	76 (56.7)	19 (44.2)	0.152
Induction	34 (25.4)	18 (41.9)	0.039
Primary Cesarean	24 (17.9)	6 (14.0)	0.547
Mode of delivery: n (%)			
Spontaneous vaginal delivery	85 (75.9)	28 (75.7)	0.979
Instrumental	7 (6.3)	1 (2.7)	0.680
Emergency Cesarean	20 (17.9)	8 (21.6)	0.611
Neonatal:			
Birth weight – gram	3846 ± 550	3648 ± 414	0.031
Birth weight percentile	76.7 (57.9–94.8)	71.6 (48.8–82.4)	0.050
Birth weight <10th percentile – n (%)	6 (4.4)	0 (0)	0.338
Birth weight >90th percentile – n (%)	48 (35.3)	7 (16.3)	0.018
Birth weight ≥4000 grams – n (%)	54 (39.7)	8 (18.6)	0.011

NEG: negative, POS: positive, GDM: gestational diabetes mellitus, BMI: body mass index, PCOS, polycystic ovarian syndrome, DM: diabetes mellitus, OGTT: oral glucose tolerance test, FAC: fetal abdominal circumference, EFW: estimated fetal weight. Data is presented as mean ± SD, median (IQR) or n (%).

* Multiparous women only.

(13.7%) had more than one OGTTs during pregnancy. We excluded 6 women due to incomplete results of the first OGTT, 3 due to unknown timing of the test, 2 women with a positive OGTT1 and 236 women with the index OGTT performed <24 or >28 weeks of pregnancy. This resulted in 183 women with a negative OGTT performed between 24–28 weeks of gestation, which was repeated in the same pregnancy. 43 women (23.5%) with either fasting or post load glucose levels above the WHO 1999 cut-off values were classified as having GDM based on the second OGTT.

Patient characteristics are shown in Table 1. Women in the non-GDM and GDM group were similar in maternal age (33 vs 35 years, $p = 0.242$) and BMI (25.5 kg/m^2 vs 28.0 kg/m^2, $p = 0.100$). Both groups were furthermore similar regarding ethnicity, rates of PCOS and method of conception. In the GDM group 36.7% of multiparous women had a history of GDM, compared to 18.4% in the non-GDM group ($p = 0.036$), with a significant OR of 2.6 (95% CI 1.0–6.3). A positive family history for diabetes mellitus was present in 31.4% in the non-GDM group and 39.5% in the GDM group ($p = 0.324$). The number of women with 1 or ≥2 risk factors for GDM were similar in both groups.

Median gestational age at time of OGTT1 was similar in both groups (25.6 weeks vs 25.3 weeks, $p = 0.631$). In the GDM group the median OGTT1 fasting plasma glucose was significantly higher compared to the non-GDM group (4.9 mmol/L vs 4.8 mmol/L, $p = 0.028$). The 2 -h post load glucose of OGTT 1 was also higher (7.1 mmol/L vs 5.7 mmol/L, $p = <0.001$) in this group. ROC curve analysis showed an optimal cut-off value for fasting glucose of 4.8 mmol/L, with sensitivity of 0.60, specificity 0.61, PPV 0.32 and NPV 0.83. The optimal cut-off value for the 2 -h post load glucose was 6.5 mmol/L, with sensitivity of 0.72, specificity 0.75, PPV 0.47 and NPV 0.90. Women with a fasting glucose >4.8 mmol/L or 2 -h post load glucose >6.5 mmol/L were at significantly higher risk for subsequent GDM diagnosis, with ORs of 2.3 (95% CI 1.2–4.8) and 7.8 (95% CI 3.6–16.7) respectively. With a pre-test probability of 23.5% for a positive second OGTT, a fasting glucose ≤4.8 mmol/L would result in a post-test probability of 16.6% and >4.8 mmol/L of 32.1%. A 2 -h post load value ≤6.5 mmol/L would result in a post-test probability of 10.2% and >6.5 mmol/L of 46.9%. Timing of the second OGTT (OGTT 2) was similar in both groups.

There were no differences in rates of fetal abdominal circumference >90th percentile, estimated fetal weight >90th percentile or polyhydramnios on ultrasound examination in both groups.

Women in the GDM group delivered earlier compared to the non-GDM group (39.3 weeks vs 39.9 weeks, $p = 0.022$) and had higher rates of induced labour (41.9% vs 25.4%, $p = 0.039$). Mode of delivery, either spontaneous vaginal, instrumental or emergency Cesarean, was similar in both groups. Absolute birth weights of neonates born from mothers in the GDM group were lower compared to the non-GDM group (3648 vs 3846 g, $p = 0.031$). Median birthweight percentile, adjusted for gestational age, gender and parity was 71.6 compared to 76.7 in the non-GDM group ($p = 0.050$). Rates of birth weight >90th percentile were significantly lower in the GDM group (16.3% vs 35.3%, $p = 0.018$), as were the rates of birth weight ≥4000 g (18.6% vs 39.7%, $p = 0.011$).

Indication for OGTT testing

Indications for OGTT1 and OGTT2 are listed in Table 2 for both the non-GDM (NEG-NEG) and GDM (NEG-POS) groups. For OGTT1, a total of 331 indications were provided for the 183 tests performed. Ethnicity was the most frequent indication: 24.1% in the GDM group and 25.0% in the non-GDM group ($p = 0.873$), followed by a BMI ≥30 kg/m^2 (20.7% and 19.3%). In some cases

Table 2
Indications for OGTT 1 and OGTT 2.

	non-GDM (NEG-NEG) n = 140	GDM (NEG-POS) n = 43	p-value
OGTT1:* n (%)			
Ethnicity	61 (25.0)	21 (24.1)	0.873
BMI >30 kg/m^2	47 (19.3)	18 (20.7)	0.773
Family history for DM	46 (18.9)	17 (19.5)	0.888
History of macrosomia	33 (13.5)	10 (11.5)	0.629
History of GDM	18 (7.4)	12 (13.8)	0.073
Fetal growth	18 (7.4)	1 (1.1)	0.032
PCOS	5 (2.0)	3 (3.4)	0.466
Elevated random glucose first trimester	5 (2.0)	0 (0)	0.331
History of intrauterine death	3 (1.2)	1 (1.1)	0.953
Maternal weight gain	2 (0.8)	1 (1.1)	1.000
Auto-immune hypothyroidism	1 (0.4)	2 (2.3)	0.170
Thirst	0 (0)	1 (1.1)	0.262
History of neonatal hypoglycemia	1 (0.4)	0 (0)	1.000
Polyhydramnios	1 (0.4)	0 (0)	1.000
Dizziness	1 (0.4)	0 (0)	1.000
Maternal age	1 (0.4)	0 (0)	1.000
History of shoulder dystocia	1 (0.4)	0 (0)	1.000
OGTT2:* n (%)			
Fetal growth**	116 (74.8)	34 (68.0)	0.342
Polyhydramnios	13 (8.4)	1 (2.0)	0.195
History of GDM	9 (5.8)	5 (10.0)	0.336
Borderline results OGTT1	5 (3.2)	4 (8.0)	0.226
Thirst	4 (2.6)	3 (6.0)	0.364
Random elevated glucose	4 (2.6)	0 (0)	0.574
Unexpected low values OGTT1	2 (1.3)	0 (0)	1.000
Dizziness	0 (0)	2 (4.0)	0.059
History of intrauterine fetal death	1 (0.6)	0 (0)	1.000
History of neonatal hypoglycemia	1 (0.6)	0 (0)	1.000
Glycosuria	0 (0)	1 (2.0)	0.244

OGTT: oral glucose tolerance test, NEG: negative, POS: positive, GDM: gestational diabetes mellitus, BMI: body mass index, DM: diabetes mellitus, PCOS: polycystic ovarian syndrome.

* Includes patients with >1 given indication for OGTT.

** Consisted of clinical suspected macrosomia or accelerated fetal growth, either based on ultrasound measurements or physical examination.

OGTTs were performed for reasons outside the regular screening protocol, such as a history of neonatal hypoglycemia, the presence of auto-immune hypothyroidism, a history of shoulder dystocia (without macrosomia) or maternal age.

For OGTT2 there were 205 indications for the 183 tests performed. Fetal growth was the most prevalent indication with 68.0% of tests in the GDM group and 74.8% in the non-GDM group performed for this reason. Of the 150 repeated OGTTs performed because of fetal growth, 34 were positive for GDM, corresponding to a positive predictive value of 22.7%. Polyhydramnios as an indication for repetition of the OGTT yielded a diagnosis of GDM in 7.1% (1/15) of cases. Repeating the OGTT because of borderline results of the index OGTT occurred in 9 cases. In these cases the 2 -h post load values of OGTT1 ranged from 7.4 to 7.7 mmol/L. There were no significant differences in frequency of reported OGTT1 and OGTT2 indications between the two groups.

Discussion

In this study we identified women with risk factors for GDM who underwent multiple oral glucose tolerance tests during pregnancy to provide insight whether repeating the test is of use after an initial negative result between 24–28 weeks of pregnancy. We demonstrated that in this group 23.5% of women were subsequently diagnosed with GDM. Fetal growth was the most common clinical indication for retesting. Factors associated with GDM diagnosis were a GDM in previous pregnancy and higher glucose values of the index OGTT, especially the 2 -h post load value.

Repeated testing, even in the late third trimester, has been shown to identify additional cases of GDM after initial normal OGTT results [3,33–36]. The reported additional yield of GDM diagnoses by repeated OGTTs ranged between 3.9% and 28.9% in studies where women were universally rescreened, irrespective of clinical symptoms [3,33–40]. In a study by Kurtbas et al. in 200 pregnant women universal screening with a 50-g glucose challenge and diagnostic 100-g OGTT was performed at 24–28 weeks and repeated at 30–34 weeks. 5.2% of women was additionally diagnosed with GDM after initial normal OGTT results [3]. Advanced maternal age and a history of macrosomia were associated risk factors. Although we observed a trend of higher median maternal age and maternal age ≥35 and ≥40 years in the GDM group in our cohort, this was not statistically significant. Also, a history of macrosomia was not a predictor for GDM in our study.

In another cohort study performed by Bitó et al., using a risk-based screening approach, OGTTs were repeated at 24–28 and 32–34 weeks of pregnancy in women with normal results <16 weeks of gestation [35]. Of the 123 women with normal results at 24–28 weeks, 39.0% tested positive for GDM at 32–34 weeks, with obesity being the most predictive risk factor. Although BMI and rates of obesity were similar to our cohort, maternal weight was not predictive for subsequent GDM in our study. The authors furthermore noted that higher glucose values of the index OGTT were predictive for GDM later in pregnancy. They concluded that the glucose values were most effective for ruling out subsequent GDM diagnosis, with high false positive rates in those exceeding the optimal thresholds. This is consistent with our findings, where the post-test probability for GDM when the index OGTT results exceed the cut-offs as described was only 46.9% at best. However, similarly to the study by Bitó et al., negative predictive values were high.

To our knowledge, this is the first study to include women with risk factors for GDM and negative OGTT screening at 24–28 weeks in which the OGTT is repeated, mostly due to clinical signs or symptoms. The strengths of this study include the multicenter sample and overview of indications for repeated testing, as provided by clinicians, to provide insight into which clinical signs are more likely to result in a diagnosis of GDM. There are also several limitations. We only included the women for analysis that were initially screened for GDM at 24–28 weeks of pregnancy. This resulted in exclusion of a substantial group of women with multiple OGTTs in a single pregnancy, for instance with an index OGTT at 22–23 weeks, and thus reducing our sample size. We used this window as this is recommended by (inter)national guidelines for GDM screening [22–24]. Another limitation is that our study group primarily consists of women with risk factors for GDM. Therefore our results may not directly apply to regions with universal screening, or with very different base-line risks for GDM. Also the use of different cut-off values to diagnose GDM in clinical practice, such as the WHO 2013 criteria [41], will have an effect on the number of both initial and subsequent GDM diagnoses in a population. Future studies are needed to evaluate the additional yield of repeated testing when clinical symptoms occur with other diagnostic criteria in use.

In our study fetal growth, mostly suspected macrosomia based on ultrasound examination, was the most common clinical symptom suggestive for GDM for which OGTTs were repeated. In a previous study by Griffin et al. it was found that macrosomia in the current pregnancy had a positive predictive value for GDM of 40% in women tested for the first time [25]. In our study in women with a prior negative test we found that macrosomia had a lower positive predictive value of 22.7% for GDM. This is, however, higher than the 5.9% of GDM cases found in a study by Geifman-Holtzman et al., consisting of 170 term women presenting with suspected macrosomia (estimated fetal weight >90th percentile or >4.000 g) in the third trimester, after an initial negative screening 50-g glucose challenge test at 24–28 weeks [42]

Interestingly, we found the rates of neonatal macrosomia (birth weight ≥4000 g) and large-for-gestational-age (birth weight >90th percentile) at birth to be about twice as high in the non-GDM compared to the GDM group. Also, the rates of LGA in the non-GDM women were much higher than expected in the general obstetric population [6]. This could indicate that with the current screening methods some form of hyperglycaemia was undetected in the non-GDM group despite the repeated negative OGTTs. This corresponds with findings from the HAPO study, in which lower glucose thresholds were already associated with risks for LGA [10].

Another finding in our study was that in the group of women with a negative screening at 24–28 weeks and positive OGTT later in pregnancy, 36.7% had a history of GDM. Given the increased risk for undiagnosed overt diabetes and recurrence of GDM, guidelines advise early screening in women with a previous GDM (first trimester or <16 weeks of gestation) [22–24], to be repeated at 24–28 weeks if normal. Currently, the detection rate and health benefits of this early screening is unknown [43–45]. The high rate of history of GDM in the women diagnosed with GDM after initial normal screening at 24–28 weeks in our study could indicate that current screening policies may not be sufficient for this high-risk group. However, since in our study not all women with a previous GDM were routinely rescreened, our findings only represent the women with an additional indication for an OGTT and not the whole group.

The OGTT is an invasive procedure, as it requires multiple venipunctures. It is furthermore associated with patient discomfort and complaints including nausea, vomiting and reactive hypoglycemia, resulting in women refusing to undergo the test [46–48]. However, the diagnosis of GDM has consequences for both the pregnant woman and her offspring, as it results in a set of actions, including intensified monitoring during pregnancy and labour, and postpartum screening for neonatal hypoglycemia, which is common in infants born from diabetic mothers [9]. Also women are advised to undergo evaluation to detect persistent

hyperglycemia postpartum, and yearly glucose evaluations because of increased risk for progression to type 2 diabetes after GDM [12,22–24]. Lastly, in a following pregnancy an additional early OGTT is recommended, possibly allowing for a more timely recognition and treatment. Therefore by diagnosing GDM, even later in pregnancy, a series of health promoting actions are undertaken which may justify a late OGTT even after a prior negative test.

Conclusion

Repeating an oral glucose tolerance test later in pregnancy after a previous negative test in women at risk still yields additional GDM cases, especially in women with a history of GDM and higher index OGTT results. Regarding the application of this study in clinical practice, the results could be used by patient and health care provider to further determine whether repeating the OGTT is acceptable compared to risks of a missed GDM diagnosis, treatment effects and long-term consequences.

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None.

Contribution to authorship

K.E.B. and A.P.v.R. contributed to the study design, data acquisition, interpretation of data, critically reviewing the drafts and the final manuscript. L.d.W. and D.B. performed data acquisition, analyses, interpretation of data, drafting and finalizing the manuscript. B.B.v.R. reviewed and critically revised the manuscript. All authors gave final approval for publication.

Declaration of Competing Interest

None of the authors have declared any potential conflict of interest regarding this study.

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None.

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