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ORIGINAL RESEARCH

Perinatal and neonatal outcomes in gestational diabetes: The importance of the number of abnormal values in an oral glucose tolerance test

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is defined by one or more abnormal values in an oral glucose tolerance test (OGTT). The significance/importance of the number of abnormal values in relation to adverse perinatal and neonatal outcomes is unclear. We assessed the association of these outcomes with the number of abnormal glucose values in a 2-h 75 g OGTT in a large register-based cohort.

Material and Methods: This sub-study of the Finnish Gestational Diabetes Study was based on the Finnish Medical Birth Register 2009 supplemented with OGTT laboratory data of 4869 pregnant women from six Finnish hospitals. The diagnostic cut-offs in OGTT according to the Finnish guidelines for plasma samples were ≥5.3 mmol/L (fasting), ≥10.0 mmol/L 1 h or ≥8.6 mmol/L 2 h after the glucose load. As per the guidelines, women with one or several abnormal OGTT values received diet and lifestyle counseling in the primary care, self-monitored their glucose values and received pharmacological therapy as needed. Women with GDM were categorized according to the number of abnormal glucose values. The primary outcomes, composites of adverse perinatal (pre-eclampsia, preterm delivery, macrosomia or primary cesarean section) and neonatal outcomes (birth trauma, neonatal hypoglycemia, hyperbilirubinemia or stillbirth/perinatal mortality), were analyzed by logistic regression adjusted for maternal age, pre-pregnancy body mass index, parity, socio-economic status and smoking.

Results: Of all the women, 877 (18.0%) had one, 278 (5.7%) two and 79 (1.6%) three abnormal OGTT values, while 3635 (74.7%) women were normoglycemic. Women with at least two abnormal OGTT values had higher proportions of adverse perinatal

Abbreviations: BMI, body mass index; CI, confidence interval; GDM, gestational diabetes; GW, weeks of gestation; IADPSG, International Association of Diabetes in Pregnancy Study Group; ICD, International Classification of Diseases; LGA, large for gestational age; MBR, Medical Birth Register; OGTT, oral glucose tolerance test; OR, odds ratio; SD, standard deviation.

For affiliations refer to page 137.

composite (35.0% vs. 27.5%, adjusted odds ratio 1.36; 95% confidence interval 1.03–1.81) and neonatal composite outcomes (31.1% vs. 18.9%, adjusted odds ratio 1.88; 95% confidence interval 1.40–2.52) compared to women with one abnormal value. The risks of delivery induction and neonatal hypoglycemia were increased regardless of the number of abnormal values when compared with normoglycemic women.

Conclusions: The risk of adverse perinatal and neonatal outcomes is significantly higher in women with two or more abnormal OGTT values than in those with one abnormal value.

KEYWORDS
composite outcomes, gestational diabetes, neonatal outcomes, oral glucose tolerance test, perinatal outcomes

1 | INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common medical conditions complicating pregnancies and is becoming more prevalent globally with prevalence rates of 11%–30%.[1] Currently, the most frequently used method to diagnose GDM is a 2-h 75 g oral glucose tolerance test (OGTT), and the diagnosis is based on one or more abnormal values in the OGTT. This was endorsed by the International Association of Diabetes in Pregnancy Study Group (IADPSG) based on the Hyperglycemia and Adverse Pregnancy Outcome study.[2,3] This recommendation is widely used around the world, and organizations, such as the World Health Organization and the International Federation of Gynecology and Obstetrics, have adopted these diagnostic criteria.[4,5]

Current guidelines do not share a consensus on whether a single abnormal OGTT value is of clinical significance or would it be cost-effective to counsel and treat only women with two or three abnormal values. Studies have reported that women with one elevated OGTT value are at risk of adverse perinatal outcomes if not counseled and treated.[6–8] On the contrary, it has also been reported that adverse pregnancy outcomes increase with the number of abnormal glucose values.[9,10]

According to the IADPSG recommendations, GDM is diagnosed after one abnormal glucose concentration in the OGTT.[2] However, the significance of a single abnormal OGTT concentration on pregnancy outcomes remains unclear. Therefore, in the present study, our aim was to compare the significance of one vs several abnormal OGTT values on pregnancy and perinatal outcomes in a large register-based cohort.

Key message

In a study setting where all women with GDM received counseling and treatment as needed, perinatal and neonatal risks were increased in women with at least two abnormal oral glucose tolerance test values compared to those with one abnormal value.

2 | MATERIAL AND METHODS

2.1 | Study population and data sources

The study has been conducted and reported applying the criteria of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[11] This study was based on data from the register-based arm of the Finnish Gestational Diabetes Study (FinnGeDi), which was initiated in conjunction with the introduction of the new national comprehensive guidelines for GDM screening, diagnosis and treatment in Finland in 2008.[12] The study has been presented in detail previously.[13] The registry data was obtained from the Medical Birth Register (MBR), maintained by the Finnish Institute of Health and Welfare which includes data on the course and complications of pregnancy and delivery and perinatal health of newborns until the age of 7 days, as well as the 10th version of International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes for medical diagnoses of the mother and child. All live births and stillbirths from $22^{0/7}$ weeks of gestation (GW) or birthweight of at least 500 grams are reported in the MBR.[14] The MBR has comprehensive coverage with high-quality data.[15,16]

The MBR also includes information on whether the OGTT was performed during pregnancy and if the result was abnormal. However, it does not include data on specific glucose concentrations. To address this, we collected numerical OGTT data from all women who delivered in 2009 and had undergone an OGTT in the laboratory in six delivery units in Finland: two tertiary level (Oulu and Tampere) and four secondary-level (Southern Karelia, Seinäjoki, Kainuu and Satakunta) hospitals, each serving a specific geographical area. Numerical OGTT data were available from these hospitals through their laboratory data system. All OGTTs performed during pregnancy between 12 and 40 GW in the years 2008 and 2009 were linked to MBR data. The linkage was performed using unique personal identification numbers by personnel uninvolved with this study. Women with the OGTT performed before 12 GW, GDM

diagnosis (ICD-code O24.4 or O24.9) or insulin treatment during pregnancy according to the MBR but normoglycemic OGTT values and multiple pregnancies were excluded from the study. In cases where the mother had two pregnancies within the same year, only the first was included. Thereafter, the study population consisted of 4869 women who underwent OGTT between 12 and 40 GW (Figure 1).

The Finnish national guidelines, published in 2008, introduced a comprehensive screening approach for GDM, replacing the previous risk factor-based screening policy.[12] According to these guidelines, all women, except those with very low risk, are recommended to be screened for GDM using a two-hour 75 g OGTT between 24 and 28 GW. The very low-risk group comprises of <25-year-old primiparous women with body mass index (BMI) <25 kg/m^2 and without family history of diabetes and <40-year-old multiparous women with BMI <25 kg/m^2 and without history of GDM or macrosomic newborn.[12,17] High-risk women (i.e., women with prior GDM, BMI >35 kg/m^2 or polycystic ovary syndrome with insulin resistance) are to undergo their first OGTT screening between 12 and 16 GW, and if the results are normal, the test is repeated between 24 and 28 GW.[12] The OGTT is performed after a 12-h overnight fast in the laboratory nearest to the woman's residence. Blood samples are drawn from the antecubital vein into fluoride citrate tubes and analyzed within 24 h in a local laboratory using commercial enzymatic assays, with the assays used varying between laboratories. The involved laboratories in the study were accredited laboratories under ISO15189:2012 standard and had quality management systems. The laboratories performed regular internal quality control checks with controls of known concentrations and were also involved in external quality control schemes. Based on the Finnish guidelines (adapted from the American Diabetes Association guidelines[18] in 2008), the diagnostic values for plasma samples are ≥5.3 mmol/L at the baseline (fasting sample), ≥10.0 mmol/L 1 h or ≥8.6 mmol/L 2 h after the glucose load.[12] Women with one or several abnormal OGTT values, as per the guidelines, receive individualized dietary and lifestyle counseling in maternity clinics and begin glucose self-monitoring thereafter. If, despite the dietary and lifestyle interventions, self-monitored plasma glucose concentrations repeatedly exceed the target levels (i.e., <5.5 mmol/L fasting and <7.8 mmol/L 1 h postprandial), pharmacological therapy is considered.

2.2 | Study outcomes

Maternal age was defined at the time of delivery, and parity was defined by the number of previous deliveries. BMI was calculated using self-reported height and weight before pregnancy, both of which were recorded at the first antenatal visit. Socioeconomic status was divided into four categories using the occupation reported in the MBR: (1) upper-level employees with administrative, managerial, professional and related occupations, (2) lower-level employees with administrative and clerical occupations, (3) manual workers and (4) others—such as stay-at-home mothers, students, pensioners and self-employed individuals. Self-reported smoking status was categorized as nonsmokers and smokers. Neonatal morbidity was evaluated by a pediatrician as per ICD-10 codes.

The primary study outcomes included composites of adverse perinatal and neonatal outcomes. Composite adverse perinatal outcome included pre-eclampsia, preterm delivery (<37$^{0/7}$ GW), macrosomia or large for gestational age (LGA) >90% (birthweight standard deviation [SD] scores over 90%) and primary cesarean section, and composite adverse neonatal outcome included birth trauma [fracture of the clavicle (P13.4), Erb's paresis (P14.0)], neonatal hypoglycemia (P70.0–70.9), hyperbilirubinemia (P59.0–59.9), and stillbirth/perinatal mortality. The choice to use composite outcomes was based on previously published articles.[19–21] The birthweight SD score is a sex-specific parameter to estimate birthweight and length in singletons and twins born at 23–43 GW to primiparous or multiparous mothers, according to Finnish standards.[22] According to the Finnish current care guidelines, glucose concentration is mandatorily measured in all newborns of GDM

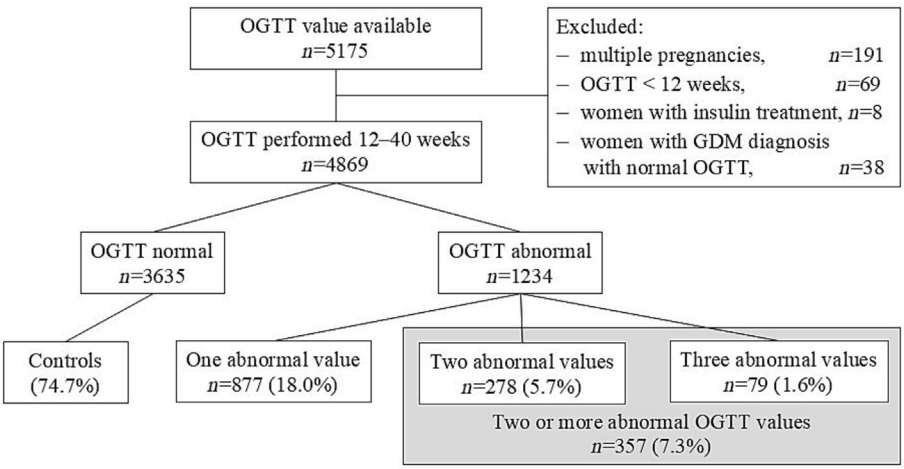

FIGURE 1 Flow chart of the study.

mothers.[12] In addition to GDM, other potential indications for neonatal glucose screening in asymptomatic newborns included preterm birth, a birth weight of <2.5 kg or >4.5 kg or maternal use of β-blockers. A diagnosis of hypoglycemia was recorded in the MBR if a newborn required any interventions for hypoglycemia including intravenous glucose, although there are no unified diagnostic criteria for neonatal hypoglycemia in Finland.

Secondary maternal outcomes included gestational hypertension and pre-eclampsia (ICD-10 codes O13 and O14 included, O10 and O11 excluded), induction of labor, Cesarean section. Secondary neonatal outcome measures included gestational age at delivery and birthweight SD scores.

2.3 | Statistical analyses

Categorical variables were reported as frequencies and percentages, and continuous variables as mean and SD. Pearson's χ^2 test was used to compare the difference in proportions of demographic variables. Independent sample *t*-test was used to compare the difference in the means of demographic data. Differences between each GDM group were tested using Fisher's exact test. Logistic and linear regression analyses were used to estimate odd ratios (ORs) with their 95% confidence intervals (CIs) and mean differences (with 95% CIs) of outcomes associated with GDM, respectively, according to the number of abnormal OGTT values. Logistic and linear regressions were also performed to estimate the differences between one or at least two abnormal glucose values. The results were adjusted for maternal age, pre-pregnancy BMI, parity category (primiparity/multiparity), socio-economic status and smoking. A two-sided *p*-value <0.05 was considered statistically significant. All statistical analyses were carried out using the SPSS 29 statistical package.

3 | RESULTS

The OGTTs were performed between 12 and 40 GW (mean 26 GW, SD 4.4) on 4869 women who delivered in 2009 in the study hospitals. OGTT was abnormal and hence GDM diagnosed in 1234 (25.3%) women, and the control group consisted of 3635 (74.7%) women with normal OGTT results. Of the women with GDM, 877 (71.1%) had one, 278 (22.5%) two and 79 (6.4%) three abnormal values in the OGTT. Women with two or three abnormal OGTT values were analyzed as one group ($n = 357$, 7.3% of all women) (Table 1).

When women with GDM were compared to normoglycemic controls, the percentage of those smoking and manual workers was higher in the GDM group. When the baseline characteristics were considered, women with at least two abnormal OGTT values had higher pre-pregnancy BMI compared to those with one abnormal OGTT value. Of the women with one abnormal OGTT value, 7.2% received insulin treatment, while the proportion in women with at least two abnormal was 16.0% (Table 1).

Perinatal and neonatal characteristics according to the number of abnormal OGTT values, and the unadjusted and adjusted ORs and risk estimates for the study outcomes are presented in Table 2 and in Figures 2 and 3. The proportions of composite perinatal (35.0% vs. 27.5%, adjusted OR (aOR) 1.36, 95% CI 1.03–1.81) and composite neonatal outcomes (31.1% vs. 18.9%, aOR 1.88, 95% CI 1.40–2.52) were higher in women with at least two abnormal OGTT values compared to women with one abnormal OGTT value. Furthermore, women with at least two abnormal OGTT values had higher number induction of labor (29.1% vs. 22.5%, aOR 1.36, 95% CI 1.02–1.82), preterm delivery (8.4% vs. 5.1%, aOR 1.75, 95% CI 1.05–2.93), primary cesarean section (19.3% vs. 14.4%, aOR 1.41, 95% CI 0.99–2.02) and neonatal hypoglycemia (21.0% vs. 11.9%, aOR 1.96, 95% CI 1.40–2.75) when compared to those with one abnormal value.

When compared to normoglycemic women, the proportions of composite perinatal (27.5% vs. 23.4%, aOR 1.20, 95% CI 1.01–1.44) and composite neonatal outcomes (18.9% vs. 9.6%, aOR 2.16, 95% CI 1.75–2.67) were higher in women with one abnormal OGTT value. Similarly, women with at least two abnormal values in the OGTT had higher proportions of composite perinatal (35.0% vs. 23.4%, aOR 1.68, 95% CI 1.30–2.16) and composite neonatal outcomes (31.1% vs. 9.6%, aOR 4.05, 95% CI 3.09–5.31) compared to normoglycemic women. Women with one abnormal OGTT value had more often pre-eclampsia, and women with at least two abnormal OGTT values had a higher proportion of gestational hypertension, preterm delivery, primary cesarean section, macrosomia, hyperbilirubinemia, when compared to normoglycemic controls. Regardless of the number of abnormal OGTT values, women with GDM had more often induction of labor and neonatal hypoglycemia.

4 | DISCUSSION

In the present study, women with two or more abnormal OGTT values had a higher risk of adverse composite perinatal and neonatal outcomes compared to women with one abnormal OGTT value, including preterm delivery, neonatal hypoglycemia and delivery induction. In addition, both GDM groups had an increased risk of delivery induction and neonatal hypoglycemia compared to the normoglycemic group. Women with two or more abnormal values also had a higher risk of preterm delivery, primary cesarean section, and hyperbilirubinemia, while women with one abnormal value had a higher risk of pre-eclampsia. These findings indicate that women with any number of abnormal OGTT values, and hence GDM, had an increased incidence of adverse perinatal and neonatal outcomes than normoglycemic controls.

The significance of one abnormal OGTT value has been debated. Some criteria—for example, Carpenter-Coustan and the National Diabetes Data Group criteria—set the diagnosis of GDM only after two or more abnormal values.[23,24] However, these screening policies were based on four glucose concentrations instead of three values measured in the IADPSG. According to the IADPSG

TABLE 1 Maternal characteristics of normoglycemic women and women with abnormal oral glucose tolerance test values.

Characteristics	Normoglycemic women	Women with one abnormal OGTT value	Women with two or more abnormal OGTT values	*p*-value, normoglycemic vs one abnormal OGTT value	*p*-value, normoglycemic vs two or more abnormal OGTT values	*p*-value, one vs two or more abnormal OGTT values
n (%)	3635 (74.7)	877 (18.0)	357 (7.3)			
Age at delivery (years), mean (SD)	29.5 (5.3)	30.3 (5.5)	30.8 (5.7)	<0.001	<0.001	0.175
Pre-pregnancy BMI (kg/m^2), mean (SD)	25.8 (4.6)	27.8 (5.7)	29.6 (6.2)	<0.001	<0.001	<0.001
Primiparity, *n* (%)	1720 (47.3)	338 (38.5)	134 (37.5)	<0.001	<0.001	0.747
Smoking, *n* (%)	437 (12.5)	137 (16.2)	60 (17.6)	0.005	0.009	0.605
Socioeconomic status, *n* (%)						
Upper-level employee[a]	630 (21.3)	137 (18.9)	52 (18.6)	0.161	0.056	0.697
Lower-level employee[b]	1219 (41.1)	305 (42.2)	112 (40.1)			
Manual worker	485 (16.3)	139 (19.2)	63 (22.6)			
Other[c]	629 (21.2)	142 (19.6)	52 (18.6)			
Insulin treatment	- (0.0)	63 (7.2)	57 (16.0)	<0.001	<0.001	<0.001

Abbreviations: BMI, body mass index; OGTT, oral glucose tolerance test; SD, standard deviation.

[a]Administrative, managerial, professional and related occupations.

[b]Administrative and clerical occupations.

[c]Students, pensioners, self-employed and other.

recommendations—which are nowadays widely used by, for example, the World Health Organization and the International Federation of Gynecology and Obstetrics—GDM is diagnosed already after one abnormal OGTT value.[4,5]

In a recent systematic review and meta-analysis, GDM was diagnosed by a three-hour 100 g OGTT after an abnormal one-hour 50 g glucose challenge test, and women with only one abnormal OGTT value remained untreated.[6] A single abnormal value, hence untreated and not defined as GDM, was associated with adverse maternal and neonatal outcomes—macrosomia, cesarean delivery, pregnancy induced hypertension, neonatal intensive care unit admission, neonatal hypoglycemia and respiratory distress syndrome. Another study, wherein GDM was diagnosed by the IADPSG criteria, reported higher risks of cesarean sections and LGA in women with any one abnormal glucose value and the risk further increased in those with more than one abnormal value.[25]

In the present study, two or more abnormal OGTT values led to an almost 2-fold higher prevalence of neonatal hypoglycemia, 1.5-fold increased prevalence of adverse composite neonatal outcomes and 2-fold increased admission to neonatal ward compared to neonates whose mothers had only one abnormal value in the OGTT. Thus, the higher number of abnormal values in the OGTT seems to have the strongest effect on neonatal morbidity. There was a 4-5-fold higher prevalence of neonatal hypoglycemia and a two-fold increased prevalence of adverse composite neonatal outcomes in women with only one abnormal OGTT value compared to normoglycemic controls. However, an increased need for care at a neonatal ward was not observed in these neonates, implying that one abnormal OGTT value could be related to an increased proportion of adverse neonatal outcomes that are relatively mild. Nevertheless, all women with GDM in this study, including those with only one abnormal OGTT value, received diet and lifestyle counseling, self-monitored their glucose values and received pharmacological treatment when indicated, and therefore should not be considered a risk-free group not requiring follow-up.

Even though the significance of one abnormal OGTT value for pregnancy outcomes seems to be less significant/important compared to several abnormal values, any degree of abnormal glucose metabolism in pregnancy has been shown to independently predict an increased risk of glucose intolerance after delivery.[9,26–28] In recent Finnish studies, incidence of type 2 diabetes mellitus and metabolic syndrome increased after delivery also in women with one abnormal OGTT value during pregnancy. The probability of these disturbances was reported to increase together with the number of abnormal OGTT values obtained during follow-up after 10 years.[29,30] Hence, regardless of the severity of glycemic disturbance during pregnancy all women with GDM should be evaluated after pregnancy for subsequent metabolic disorders.

There are several strengths in the present study. Our study included a large cohort with comprehensive data. The coverage of the Finnish national registries, especially MBR, is complete consisting of very high-quality data.[15,16] Nonetheless, there are certain limitations. The power to estimate rare severe outcomes (such as perinatal mortality, Erb's paresis) was insufficient. There may be some uncertainty in the detection of neonatal hypoglycemia due to a lack of nationally unified diagnostic criteria in Finland. Only women with the OGTT were included and hence women with very low risk of GDM and therefore no OGTT performed, according to the national guidelines, were not included. In addition, the comparison of abnormal

TABLE 2 Perinatal characteristics of normoglycemic women and women with abnormal oral glucose tolerance test values.

Characteristics	Normoglycemic women, *n* (%)	Women with one abnormal OGTT value, *n* (%)	Women with two or more abnormal OGTT values, *n* (%)	Normoglycemic vs one abnormal OGTT value, OR (95% CI), aOR (95% CI)	Normoglycemic vs two or more abnormal OGTT values, OR (95% CI), aOR (95% CI)	One vs two or more abnormal OGTT values, OR (95% CI), aOR (95% CI)
	3635 (74.7)	877 (18.0)	357 (7.3)			
Composite perinatal outcome[a]	849 (23.4)	241 (27.5)	125 (35.0)	1.24 (1.05–1.47) 1.20 (1.01–1.44)	1.77 (1.40–2.23) 1.68 (1.30–2.16)	1.42 (1.09–1.85) 1.36 (1.03–1.81)
Pre-eclampsia[b]	74 (2.0)	29 (3.3)	8 (2.2)	1.65 (1.06–2.55) 1.77 (1.12–2.79)	1.10 (0.53–2.31) 1.09 (0.49–2.46)	0.66 (0.30–1.48) 0.58 (0.25–1.37)
Preterm delivery	144 (3.9)	45 (5.1)	30 (8.4)	1.31 (0.93–1.85) 1.35 (0.94–1.94)	2.22 (1.48–3.35) 2.34 (1.49–3.68)	1.70 (1.05–2.74) 1.75 (1.05–2.93)
Macrosomia (LGA >90%)	343 (9.4)	88 (10.0)	49 (13.7)	1.07 (0.84–1.37) 0.99 (0.76–1.28)	1.53 (1.11–2.11) 1.38 (0.98–1.95)	1.43 (0.99–2.08) 1.33 (0.90–1.97)
Primary cesarean section	437 (12.0)	126 (14.4)	69 (19.3)	1.23 (0.99–1.52) 1.23 (0.97–1.55)	1.75 (1.32–2.32) 1.74 (1.27–2.39)	1.43 (1.03–1.97) 1.41 (0.99–2.02)
Composite neonatal outcome[c]	349 (9.6)	166 (18.9)	111 (31.1)	2.20 (1.80–2.69) 2.16 (1.75–2.67)	4.25 (3.31–5.45) 4.05 (3.09–5.31)	1.93 (1.46–2.56) 1.88 (1.40–2.52)
Birth trauma	46 (1.3)	13 (1.5)	8 (2.2)	1.13 (0.64–2.01) 1.14 (0.63–2.06)	1.68 (0.83–3.44) 1.84 (0.87–3.88)	1.49 (0.64–3.43) 1.65 (0.71–3.87)
Neonatal hypoglycemia	93 (2.6)	104 (11.9)	75 (21.0)	5.12 (3.83–6.85) 5.06 (3.73–6.86)	10.13 (7.30–14.05) 9.79 (6.82–14.03)	1.98 (1.43–2.74) 1.96 (1.40–2.75)
Hyperbilirubinemia	211 (5.8)	65 (7.4)	39 (10.1)	1.29 (0.97–1.73) 1.27 (0.94–1.71)	1.99 (1.39–2.85) 1.81 (1.22–2.69)	1.53 (1.01–2.33) 1.43 (0.92–2.21)
Still birth/perinatal death	8 (0.2)	2 (0.2)	2 (0.6)	-	-	-
Secondary maternal outcomes						
Pregnancy induced hypertension[d]	234 (6.4)	69 (7.9)	34 (9.5)	1.24 (0.94–1.64) 1.18 (0.88–1.57)	1.53 (1.05–2.23) 1.24 (0.82–1.87)	1.23 (0.80–1.90) 1.08 (0.69–1.71)
Induction of labor	594 (16.3)	197 (22.5)	104 (29.1)	1.48 (1.23–1.78) 1.30 (1.07–1.57)	2.10 (1.65–2.69) 1.76 (1.35–2.28)	1.42 (1.08–1.87) 1.36 (1.02–1.82)
Cesarean section (primary+secondary)	565 (15.6)	168 (19.0)	94 (25.9)	1.29 (1.06–1.56) 1.15 (0.94–1.41)	1.94 (1.51–2.50) 1.58 (1.19–2.09)	1.51 (1.13–2.02) 1.33 (0.97–1.83)
Secondary neonatal outcomes				**B coefficient (95% CI)** **Adjusted coefficient (95% CI)**	**B coefficient (95% CI)** **Adjusted coefficient (95% CI)**	**B coefficient (95% CI)** **Adjusted coefficient (95% CI)**
Gestational age at delivery, weeks mean (SD)	39.9 (1.6)	39.6 (1.7)	39.2 (2.1)	−0.08 (−0.43–-0.20) −0.08 (−0.44–-0.20)	−0.13 (−0.94–-0.58) −0.13 (−0.90–-0.53)	−0.11 (−0.66–-0.22) −0.11 (−0.63–-0.20)
Birthweight, SD score	−0.02 (1.02)	0.04 (1.00)	0.14 (1.20)	0.08 (0.00–0.15) 0.06 (−0.02–0.14)	0.20 (0.09–0.32) 0.16 (0.04–0.29)	0.12 (−0.01–0.26) 0.12 (−0.02–0.26)

Note: Adjusted for maternal age, pre-pregnancy body mass index, parity category, socio-economic status and smoking.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OGTT, oral glucose tolerance test; OR, odds ratios, SD, standard deviation.

[a]Pre-eclampsia, preterm delivery, LGA > 90% and primary cesarean section.

[b]ICD-10: O14 included, O10 and O11 excluded.

[c]Birth trauma (fracture of the clavicle, Erb's paresis), neonatal hypoglycemia, hyperbilirubinemia and stillbirth/perinatal mortality.

[d]ICD-10: O13 included, O10, and O11 excluded.

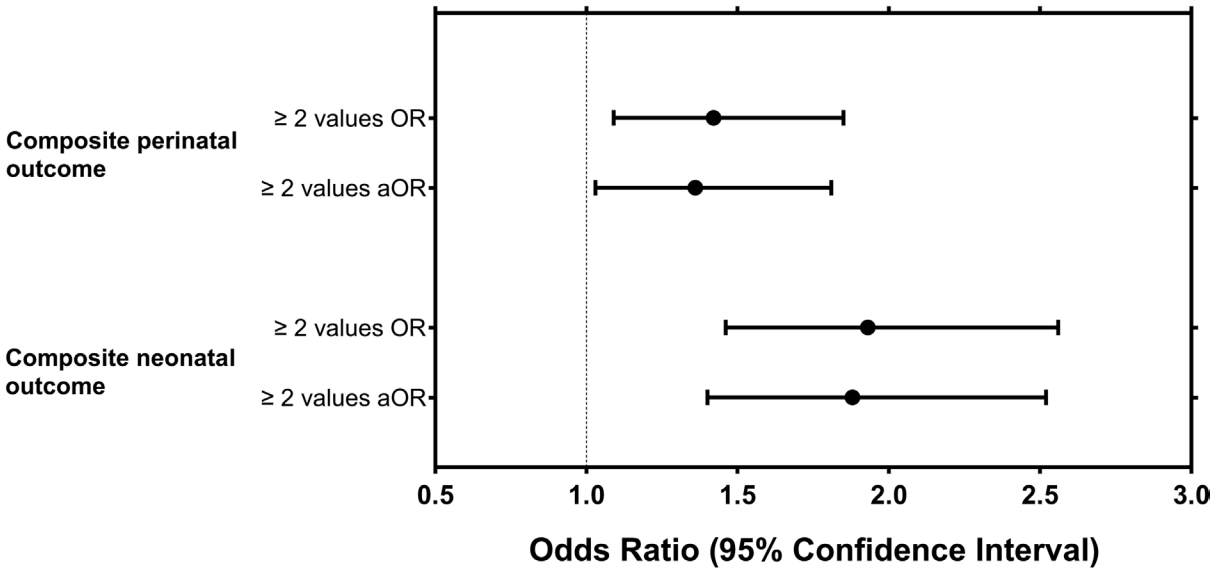

FIGURE 2 Odds ratios (ORs) and 95% confidence intervals (CIs) for the composite adverse perinatal and neonatal outcomes in women with two or more abnormal OGTT values compared to women with one abnormal OGTT value. aOR, adjusted odds ratio; OR, odds ratios. Adjusted for maternal age, pre-pregnancy body mass index, parity category, socio-economic status, and smoking. Composite adverse perinatal outcome included pre-eclampsia, preterm delivery, macrosomia and primary cesarean section, and composite adverse neonatal outcome included birth trauma (fracture of the clavicle or Erb's paresis), neonatal hypoglycemia, hyperbilirubinemia, and stillbirth/perinatal mortality.

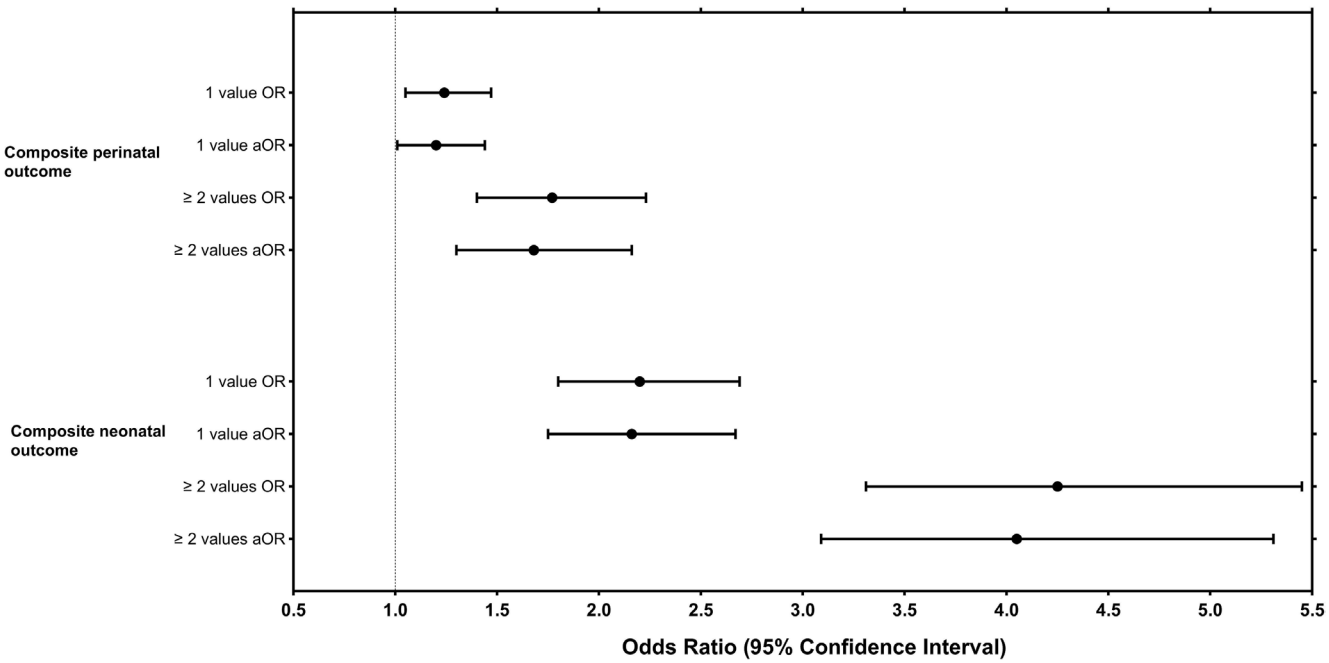

FIGURE 3 Odds ratios (ORs) and 95% confidence intervals (CIs) for the composite adverse perinatal and neonatal outcomes in women according to the number of abnormal OGTT values compared to normoglycemic controls. aOR, adjusted odds ratio; OR, odds ratios. Adjusted for maternal age, pre-pregnancy body mass index, parity category, socio-economic status and smoking. Composite adverse perinatal outcome included pre-eclampsia, preterm delivery, macrosomia and primary cesarean section, and composite adverse neonatal outcome included birth trauma (fracture of the clavicle or Erb's paresis), neonatal hypoglycemia, hyperbilirubinemia, and stillbirth/perinatal mortality.

fasting or postprandial glucose values was not evaluated in the present study.

5 | CONCLUSION

Adverse perinatal and neonatal risks are higher in women with two or more abnormal OGTT values than in women with one abnormal OGTT value. Women with any number of abnormal OGTT values are at an increased risk of induced labor, and their newborns have hypoglycemia more often than controls. However, the risk of preterm delivery, primary cesarean section, and hyperbilirubinemia is increased only if two or more values are abnormal. Of note, women with one abnormal OGTT value also received counseling and self-monitored their glucose values and therefore should not be considered as a risk-free group not requiring follow-up.

AUTHOR CONTRIBUTIONS

Sanna Eteläinen contributed to the conceptualization and conduct of the study, data analysis and drafting of the manuscript. Elina Keikkala contributed to the conceptualization and critically reviewing the manuscript. Shilpa Lingaiah contributed to data analysis, visualization and reviewing and editing the manuscript. Matti Viljakainen, Tuija Männistö, Anneli Pouta, Risto Kaaja, Johan G Eriksson, Hannele Laivuori, Mika Gissler and Eero Kajantie contributed to critically reviewing the manuscript. Marja Vääräsmäki contributed to the conceptualization and conduct of the study, and critically reviewing the manuscript. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interests.

ETHICS STATEMENT

The study was approved by the regional ethics committee of the Northern Ostrobothnia Hospital District and the Finnish Institute for Health and Welfare (Reference no. 2008/43) on June 19, 2008. According to the Finnish legislation, informed consent from study participants is not required when using anonymous register-data.

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