Lifestyle Intervention in Danish Obese Pregnant Women With Early Gestational Diabetes Mellitus According to WHO 2013 Criteria Does Not Change Pregnancy Outcomes: Results From the LiP (Lifestyle in Pregnancy) Study

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OBJECTIVE

To study effects of lifestyle intervention on metabolic and clinical outcomes in obese women fulfilling the World Health Organization (WHO) 2013 diagnostic criteria for gestational diabetes mellitus (GDM) in early gestation.

RESEARCH DESIGN AND METHODS

Secondary analysis of data from the Lifestyle in Pregnancy (LiP) study, a lifestyle randomized controlled trial in 304 pregnant women with BMI ≥30 kg/m^2. Early GDM (week 12–15) was diagnosed according to modified WHO 2013 GDM criteria: fasting venous plasma glucose ≥5.1 mmol/L and/or 2-h capillary blood glucose (CBG) ≥8.5 mmol/L (75-g oral glucose tolerance test [OGTT]). Women with treated GDM fulfilling local Danish GDM criteria (2-h CBG ≥9.0 mmol/L) (*n* = 16) and women with normal OGTT (*n* = 198) were excluded.

RESULTS

Of 90 women with early GDM, 36 received lifestyle intervention and 54 standard care. All were Caucasian, and median age was 29 years (interquartile range 27–33) and BMI 34.5 kg/m^2 (32.3–38.1). All baseline characteristics were similar in the lifestyle intervention and standard care groups. At gestational week 28–30, the women in the lifestyle intervention group had significantly higher fasting total cholesterol and fasting LDL. All other metabolic parameters including measurements of glucose, insulin, and HOMA of insulin resistance were similar. There were more planned cesarean sections in the lifestyle intervention group (22.2 vs. 5.6%), but all other obstetric outcomes were similar.

CONCLUSIONS

Lifestyle intervention in obese women fulfilling WHO 2013 GDM criteria in early pregnancy was not effective in improving obstetric or metabolic outcomes. Future studies should focus on interventions starting prepregnancy.

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New criteria for gestational diabetes mellitus (GDM) based on perinatal outcomes were proposed by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) in 2010 (1) and later endorsed by the World Health Organization (WHO) (2). The diagnostic thresholds were consensus based, drawing substantially on results from a large observational multicenter study, the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study (3), and two large randomized controlled trials (RCTs) on GDM treatment: the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) (4) and the American Maternal–Fetal Medicine Units Network (MFMUN) study (5).

A later article from IADPSG stated that the diagnostic thresholds should not be directly applied to early pregnancy because of physiological changes in fasting glucose during pregnancy (6). In addition, evidence for treatment of GDM was based on third-trimester diagnosis. However, the official WHO 2013 GDM guideline states that GDM diagnostic criteria may be applied anytime during pregnancy (2). GDM according to the WHO 2013 GDM criteria is diagnosed by a fasting plasma glucose ≥5.1 mmol/L, 1-h plasma glucose ≥10.0 mmol/L, and/or 2-h plasma glucose ≥8.5 mmol/L during a 75-g oral glucose tolerance test (OGTT).

To our knowledge, no RCT has been published addressing treatment of women with hyperglycemia in early pregnancy according to WHO 2013 GDM criteria. In the European Vitamin D & Lifestyle Intervention for Gestational Diabetes Mellitus Prevention (DALI) study, obese pregnant women received lifestyle interventions or standard care. Women diagnosed with WHO 2013 GDM criteria before 20 weeks of gestation were excluded, preventing consideration of whether this group would have benefited from intervention in terms of improved maternal metabolic profile and/or better obstetric outcome (7). In similar lifestyle intervention studies such as the Finnish Gestational Diabetes Prevention Study (RADIEL) (8) and the randomized controlled UK Pregnancies Better Eating and Activity Trial (UPBEAT) (9), exclusion criteria for hyperglycemia in early pregnancy did not follow WHO 2013 GDM criteria.

In the Lifestyle in Pregnancy (LiP) study, we reported outcomes in 304 obese pregnant women randomized to lifestyle intervention or a control group. Women with clinically diagnosed GDM at inclusion by Danish criteria (2-h capillary blood glucose [CBG] ≥9.0 mmol/L after a 75-g glucose load) were excluded from the study (10). All venous plasma measurements including fasting glucose were blinded to the clinicians. The current post hoc secondary analysis examines the effects of lifestyle intervention on metabolic and clinical outcomes in LiP women retrospectively classified using the WHO 2013 diagnostic criteria for GDM in early gestation.

RESEARCH DESIGN AND METHODS

This article focuses on the effect of lifestyle intervention in a group of women fulfilling the diagnostic WHO 2013 GDM criteria in early pregnancy (fasting venous plasma glucose [FVPG] ≥5.1 mmol/L and/or a CBG ≥8.5 mmol/L at 2 h after a 75-g OGTT). One-hour OGTT glucose values were not available in this study.

The LiP study was approved by the local ethics committee of the Region of Southern Denmark (S-20070058) and registered at ClinicalTrials.gov as NCT00530439.

Obese pregnant women were included at gestational age (GA) 12–15 weeks in two Danish university hospitals (Odense and Aarhus). Inclusion criteria were singleton pregnancy, age 18–40 years, and BMI of 30–45 kg/m^2 (calculated from the prepregnancy weight or first measured weight in pregnancy). Exclusion criteria were prior serious obstetric complications, major medical disorders including pregestational diabetes, alcohol abuse, or non-Danish speaking. A more detailed description of the study and the procedure for randomization have previously been published (10,11). The intervention consisted of two major components: dietary counseling and physical activity. Throughout pregnancy, the intervention group received four separate diet counseling sessions with a trained dietitian. Women in the intervention group were encouraged to be moderately physically active 30–60 min daily and were equipped with a pedometer to motivate and improve daily activity. Women in this group also had free full-time membership in a fitness center for 6 months until delivery, where they had closed exercise classes with a physiotherapist 1 h weekly. Training consisted of aerobic (low-step) training, training with light weights and elastic bands, and balance exercises. During pregnancy, the intervention and control groups were monitored with fasting blood samples, OGTTs, sonographic fetal biometry, and measurements of maternal weight and blood pressure. GDM was diagnosed and treated only if the 2-h OGTT CBG result was ≥9.0 mmol/L, following Danish national recommendations. The 9.0 mmol/L threshold for GDM in Danish women was based on capillary whole-blood glucose, and the venous plasma equivalent is 9.0 mmol/L. A baseline questionnaire provided information about previous pregnancies, dietary and smoking habits, and socioeconomic status.

Outcomes

Blood samples were collected from the antecubital vein. A 2-h 75-g OGTT after an overnight fast was performed three times during pregnancy (GA 12–15 [baseline], 28–30, and 34–36 weeks). Women with a diagnosis of GDM at GA 28–30 weeks were not tested again with an OGTT at GA 34–36 weeks. In this secondary analysis, we therefore only present results from the two first measurements. FVPG was measured using an enzymatic reference method with hexokinase (Integra 700; Roche, Basel, Switzerland). Two-hour CBG at the OGTT (2-h CG) was measured photometrically in a HemoCue analyzer (HemoCue, Ängelholm, Sweden).

Serum insulin concentrations were analyzed by time-resolved fluoro-immunoassay (AutoDELFIA; Wallac Oy, Turku, Finland). For insulin, the total coefficient of variation was 6.5%. Insulin was measured in picomoles per liter and converted to milliunits per liter by dividing by the conversion factor of 6 (12) Insulin resistance was estimated using HOMA of insulin resistance (HOMA-IR) as described by Matthews et al. (13) and calculated with the following formula: (fasting plasma insulin in mU/mL × fasting plasma glucose in mmol/mL)/22.5. ΔHOMA-IR was calculated by subtracting HOMA-IR at baseline from HOMA-IR at GA 28–30 weeks.

Plasma concentrations of total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were determined (Modular; Roche Diagnostics). Gestational weight gain (GWG) was calculated as weight at the 35-week visit minus weight measured at recruitment to the study.

GWG ≥9 kg was considered excessive, following the Institute of Medicine guidelines on weight gain in pregnancy (14).

Statistical Analyses

All analyses were conducted using STATA, version 14.0, software (StataCorp, College Station, TX). Differences between groups were analyzed with χ^2 test for categorical variables. Student *t* test was used for continuous variables with normal distribution; otherwise, Mann-Whitney *U* test was used. A significance level of 0.05 (two sided) was used.

RESULTS

The distribution of LiP participants according to GDM diagnosis in early pregnancy is shown in Fig. 1. The original LiP study included 304 women (150 in the intervention arm and 154 in the control arm). Of these, 16 women were excluded from this analysis, as they fulfilled Danish criteria for GDM at some stage of pregnancy and were treated accordingly. At the early OGTT (GA 12–15 weeks), 198 of 288 women had normal glucose results by WHO 2013 GDM standards. The remaining 90 women had GDM according to WHO 2013 (36 in the intervention group and 54 in the control group), with 97% diagnosed based on their fasting glucose value. The present analysis focuses on the effect of lifestyle intervention in these 90 women.

Baseline Characteristics

Women with early GDM by WHO 2013 standards were more obese (median BMI 34.5 vs. 33.0 kg/m^2; $P < 0.001$) compared with those without. Age, ethnicity, parity, smoking, and socioeconomic factors were similar between the early GDM and nonearly GDM groups (Supplementary Table 1). Women with early WHO 2013 GDM had significantly higher levels of FVPG, 2-h CG, fasting insulin, HOMA-IR, and LDL cholesterol (late pregnancy only) and lower levels of HDL cholesterol, whereas ΔHOMA-IR, fasting triglycerides, GWG, and all clinical outcomes were similar in the two groups (Supplementary Tables 2 and 3).

Early GDM

Maternal baseline characteristics were comparable in intervention and control groups (Table 1).

Metabolic measures during pregnancy are given in Table 2. At GA 28–30, women in the intervention group had significantly higher fasting total cholesterol (median 6.30 vs. 5.95 mmol/L; *P* = 0.02) and fasting LDL cholesterol (median 3.70 vs. 3.30 mmol/L; *P* = 0.02) and significantly lower fasting triglycerides (median 2.11 vs. 2.31 mmol/L; *P* = 0.03) compared with the control group. Fasting triglycerides were also significantly lower in the intervention group at baseline (median 1.24 vs. 1.44 mmol/L; *P* = 0.02). All other measures including FVPG, 2-h CG, fasting insulin, HOMA-IR, ΔHOMA-IR between baseline and second trimester and fasting, total cholesterol, LDL, and HDL were similar at baseline and GA 28–30 weeks.

Obstetric and neonatal outcomes are presented in Table 3. There were more planned cesarean sections in the intervention group (22.2 vs. 5.6%). Otherwise, there were no significant differences between rates of emergency cesarean section, hypertensive disorders, preterm delivery, large for gestational age, macrosomia, shoulder dystocia, or admission to neonatal intensive care unit in women randomized to lifestyle intervention compared with control subjects. Regarding compliance with the intervention, overall 92% of the women completed all four dietetic counseling sessions and a total of 98% completed at least three sessions. The mean attendance for the 20 aerobic classes was 10.4 h, and 56% of women in the intervention group attended the aerobic classes for at least half of the lessons.

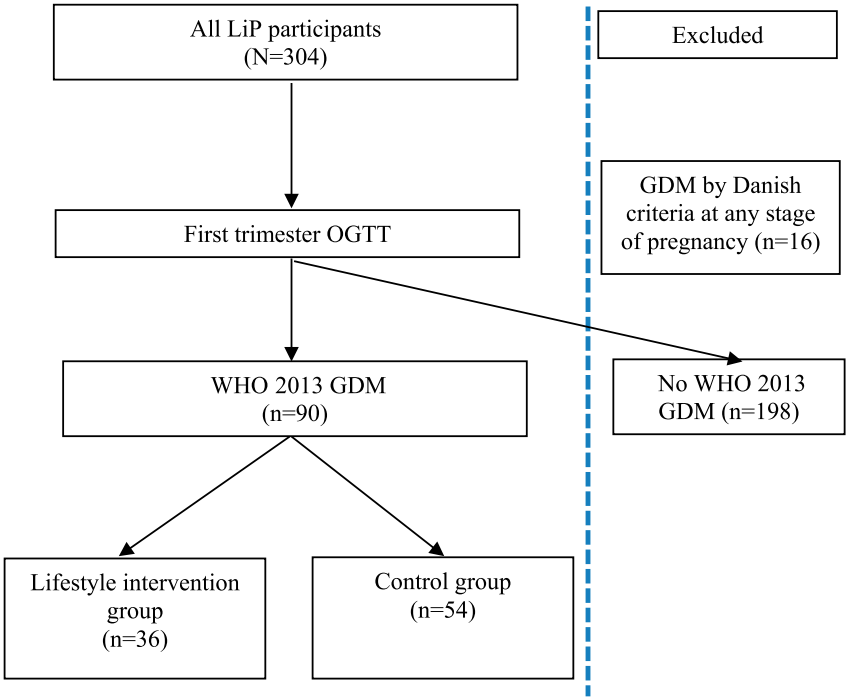

Figure 1—Flowchart of participants in the LiP study with and without first-trimester GDM according to WHO 2013 GDM criteria.

CONCLUSIONS

To our knowledge, this is the first RCT to report the effects of lifestyle intervention in obese women with GDM in early pregnancy classified according to WHO 2013 GDM diagnostic criteria. We saw no overall effect of lifestyle intervention on clinical or metabolic outcomes in women with GDM by WHO 2013 criteria at any time during pregnancy.

This study had some strengths. At the time of the study, the WHO 2013 GDM criteria were not known, and thus only the 2-h CG from the OGTT was used to determine clinical care. Thus, both participants and health professionals were blinded to GDM status by WHO 2013 criteria.

This study had some limitations. This secondary analysis was not planned as part of the original aim of the LiP study, and the numbers are small and thus not sufficiently powered to fully analyze this subgroup. As reported earlier, the

Table 1—Maternal characteristics for women included in the LiP study according to GDM in the first trimester by WHO 2013 GDM criteria

	All	Intervention	Control	
First-trimester GDM*	*n* = 90	*n* = 36	*n* = 54	*P*
Maternal characteristics				
Age (years)	29 (27–33)	29 (27–34)	30 (27–32)	0.90
BMI (kg/m^2)	34.5 (32.3–38.1)	34.3 (32.3–39.2)	34.6 (32.7–37.3)	0.29
Caucasian ethnicity (%)	100	100	100	NA
Primiparity	48 (53.0)	21 (58.3)	27 (50.0)	0.44
GWG (kg)†	7.3 (4.7–10.7) (*n* = 88)	6.4 (4.3–9.3) (*n* = 35)	8.1 (4.9–11.4) (*n* = 53)	0.20
Excessive GWG (>9 kg)	34 (38.6) (*n* = 88)	9 (25.7) (*n* = 35)	25 (47.2) (*n* = 53)	0.04
School ≥12 years	62 (68.9)	27 (75.0)	35 (64.8)	0.31
Further education ≥3 years	37 (41.1)	16 (44.4)	21 (38.9)	0.60
Gainfully employed	63 (70.0)	25 (69.4)	38 (70.4)	0.93
Smoking in pregnancy by inclusion	10 (11.1)	5 (13.9)	5 (9.3)	0.49
Diagnosed based on FVPG	87 (96.7)	35 (97.2)	52 (96.3)	0.81
Diagnosed based on 2-h value	8 (8.9)	2 (5.6)	6 (11.1)	0.38
Diagnosed based on both FVPG and 2-h value	6 (67)	1 (2.9)	5 (9.6)	0.24

Data are presented as median (interquartile range) or *n* (%), with or without *n* data in parentheses, unless otherwise indicated. NA, not applicable. *WHO 2013 GDM criteria (FVPG ≥5.1 mmol/L and/or 2-h CBG ≥8.5 mmol/L) in first trimester. †Weight at 34–36 weeks minus weight at 10–12 weeks.

women participating in the LiP study were obese but otherwise healthy. Their relatively healthy metabolic profile may have reduced the differences between the two groups. Unfortunately we have no information regarding maternal glucose in daily life outside OGTT visits. Both lifestyle intervention (similar to that received by the intervention group in LiP) and self-monitoring of blood glucose (SMBG) are the key components in the standard GDM treatment in Denmark. LiP

Table 2—Maternal metabolic measures in women included in the LiP study according to GDM in first trimester by WHO 2013 criteria

	All	Intervention	Control	
First-trimester GDM*	*n* = 90	*n* = 36	*n* = 54	*P*
FVPG (mmol/L)				
GA 12–15 weeks	5.20 (5.10–5.40) (*n* = 90)	5.30 (5.10–5.45) (*n* = 36)	5.20 (5.20–5.40) (*n* = 54)	0.32
GA 28–30 weeks	5.10 (4.80–5.50) (*n* = 87)	5.30 (4.80–5.50) (*n* = 35)	5.10 (4.80–5.50) (*n* = 52)	0.85
2-h CBG (mmol/L)				
GA 12–15 weeks	6.45 (5.90–7.50) (*n* = 86)	6.25 (5.80–7.20) (*n* = 34)	6.70 (5.90–7.55) (*n* = 52)	0.09
GA 28–30 weeks	6.55 (5.85–7.35) (*n* = 84)	6.70 (5.80–7.60) (*n* = 35)	6.50 (5.90–7.20) (*n* = 49)	0.53
Fasting insulin (mU/L)				
GA 12–15 weeks	11.50 (8.83–16.50) (*n* = 89)	14.08 (9.75–19.17) (*n* = 36)	11.17 (8.83–15.67) (*n* = 53)	0.22
GA 28–30 weeks	14.83 (11.33–20.67) (*n* = 87)	14.83 (10.83–22.33) (*n* = 35)	15.33 (11.75–20.33) (*n* = 52)	0.59
HOMA-IR				
GA 12–15 weeks	2.68 (2.08–3.99) (*n* = 89)	3.25 (2.26–4.68) (*n* = 36)	2.53 (2.04–3.81) (*n* = 53)	0.18
GA 28–30 weeks	3.30 (2.59–4.80) (*n* = 87)	3.16 (2.44–5.42) (*n* = 35)	3.38 (2.66–4.74) (*n* = 52)	0.71
ΔHOMA-IR 12–28 weeks	0.62 (−0.04 to 1.27) (*n* = 87)	0.59 (−0.13 to 1.12) (*n* = 35)	0.80 (−0.04 to 1.42) (*n* = 52)	0.62
Fasting total cholesterol (mmol/L)				
GA 12–15 weeks	5.1 (4.7–5.3) (*n* = 88)	5.2 (4.5–5.6) (*n* = 35)	4.9 (4.7–5.2) (*n* = 53)	0.15
GA 28–30 weeks	6.10 (5.50–6.60) (*n* = 87)	6.30 (5.70–6.80) (*n* = 35)	5.95 (5.40–6.45) (*n* = 52)	0.02
ΔCholesterol 12–28 weeks	1.00 (0.70–1.30) (*n* = 85)	1.10 (0.80–1.40) (*n* = 34)	1.00 (0.60–1.30) (*n* = 51)	0.07
Fasting HDL (mmol/L)				
GA 12–15 weeks	1.68 (1.41–1.96) (*n* = 88)	1.84 (1.48–1.84) (*n* = 35)	1.59 (1.39–1.84) (*n* = 53)	0.06
GA 28–30 weeks	1.71 (1.43–2.02) (*n* = 86)	1.85 (1.52–2.05) (*n* = 35)	1.61 (1.41–1.94) (*n* = 51)	0.10
ΔHDL 12–28 weeks	0.03 (−0.13 to 0.19) (*n* = 84)	0.02 (−0.08 to 0.11) (*n* = 34)	0.05 (−0.14 to 0.19) (*n* = 50)	0.66
Fasting LDL (mmol/L)				
GA 12–15 weeks	2.80 (2.50–3.10) (*n* = 88)	3.00 (2.50–3.20) (*n* = 35)	2.80 (2.40–3.00) (*n* = 53)	0.21
GA 28–30 weeks	3.55 (2.90–3.90) (*n* = 86)	3.70 (3.30–4.10) (*n* = 35)	3.30 (2.70–3.80) (*n* = 51)	0.02
ΔLDL 12–28 weeks	0.60 (0.30–0.90) (*n* = 84)	0.75 (0.40–1.10) (*n* = 34)	0.55 (0.20–0.90) (*n* = 50)	0.03
Fasting triglycerides (mmol/L)				
GA 12–15 weeks	1.39 (1.12–1.87) (*n* = 88)	1.24 (0.93–1.74) (*n* = 35)	1.44 (1.24–1.96) (*n* = 53)	0.02
GA 28–30 weeks	2.16 (1.80–2.74) (*n* = 86)	2.11 (1.62–2.52) (*n* = 35)	2.31 (1.86–3.00) (*n* = 51)	0.03
ΔTriglycerides 12–28 weeks	0.71 (0.49–1.21) (*n* = 84)	0.72 (0.53–1.08) (*n* = 34)	0.71 (0.44–1.44) (*n* = 50)	0.33

Data are presented as median (interquartile range) with *n* data in parentheses. Differences were tested with Students *t* test or Mann-Whitney *U* test where appropriate. *WHO 2013 GDM criteria (FVPG ≥5.1 mmol/L and/or 2-h CBG ≥8.5 mmol/L) in first trimester.

Table 3—Obstetric and neonatal outcomes in women included in the LiP study according to GDM in first trimester by WHO 2013 criteria

	All	Intervention	Control	
First-trimester GDM*	*n* = 90	*n* = 36	*n* = 54	*P*
Obstetric outcomes				
PIH	13 (14.4)	4 (11.1)	9 (16.7)	0.46
PE	5 (5.6)	2 (5.6)	3 (5.6)	0.92
PIH + PE	18 (20.0)	6 (16.7)	12 (22.2)	0.52
Cesarean section planned	11 (1,229)	8 (22.2)	3 (5.6)	0.02
Cesarean section emergency	13 (14.4)	4 (11.1)	9 (16.7)	0.46
Cesarean section total	24 (26.7)	12 (33.3)	12 (22.2)	0.24
GA (days)	283 (273–289)	280 (273–289)	285 (273–289)	0.53
Shoulder dystocia	1 (1.0)	0	1 (1.9)	0.41
Neonatal outcomes				
Male fetus	49 (54.4)	22 (61.1)	27 (50.0)	0.11
Preterm birth (<GA 37 weeks)	4 (4.4)	2 (5.6)	2 (3.7)	0.68
Birth weight (g)	3,657 (3,366–4,172)	3,865 (3,508–4,136)	3,575 (3,300–4,178)	0.72
Birth weight *z* score	0.28 (−0.48 to 0.98)	0.34 (−0.22 to 1.10)	0.24 (−0.56 to 0.97)	0.66
Birth weight ≥4,000 g	29 (32.2)	13 (36.1)	16 (29.6)	0.52
Birth weight ≥4,500 g	3 (3.3)	0	3 (5.6)	0.15
LGA	15 (16.7)	7 (19.4)	8 (14.8)	0.56
Abdominal circumference (cm)	34 (32–35)	34 (34–36)	34 (32–35)	0.88
Cord blood C-peptide (pmol/L)	496 (326–613) (*n* = 30)	592 (464–820) (*n* = 12)	433 (324–545) (*n* = 19)	0.17
Cord blood C-peptide ≥90 centile	10 (33.3)	7 (63.6)	3 (15.79)	<0.01
NICU admission	15 (16.7)	5 (13.9)	10 (18.5)	0.56

Data are presented as median (interquartile range), with or without *n* data in parentheses, or *n* (%) unless otherwise indicated. Differences are tested with χ^2 test, Student *t* test, or Mann-Whitney *U* test where appropriate. LGA, large for gestational age; NICU, neonatal intensive care unit; PE, preeclampsia; PIH, pregnancy-induced hypertension. *WHO 2013 GDM criteria (FVPG ≥5.1 mmol/L and/or 2-h CBG ≥8.5 mmol/L) in first trimester.

study women without a clinical diagnosis of GDM did not use SMBG, and this might be an important missing factor in our intervention group in this analysis. We have no evidence about which treatment component (diet, exercise, or SMBG) is most effective in reducing complications and regulating blood glucose (15). Similarly, we have only sparse knowledge about which type of exercise is optimal in GDM treatment (16). HbA_{1c} reflects the mean blood glucose over time but was not measured in our study. Based on results from this study, we are not able to address whether earlier or even preconception intervention would have any impact on adverse outcomes and development of GDM.

In theory, improving maternal glucose metabolism by treatment of hyperglycemia in early pregnancy may prevent macrosomia, hypertensive disorders in pregnancy, preterm delivery, and other pregnancy complications. In line with this, the "fetal glucose steal phenomenon" has been proposed. According to this theory, elevated maternal glucose can alter the fetal insulin response, resulting in increased glucose flux across the placenta despite normalization of maternal glucose in later pregnancy (17). The influence of maternal hyperglycemia in early pregnancy is supported by an observational study from New Zealand where women with slightly elevated first-trimester HbA_{1c} had increased risk of adverse obstetric outcomes (18,19). Another study from Cambridge reported that random glucose measurements in early pregnancy were highly predictive of later GDM (20). Thus, alternatives to OGTT in early pregnancy should be considered.

We found a high prevalence of GDM by WHO 2013 criteria in early pregnancy: 106 of 304 = 35% (90 women with untreated GDM by WHO 2013 plus the 16 women with treated GDM according to Danish criteria). Our results are in accordance with the findings in the European multicenter DALI study where obese (BMI ≥29 kg/m^2) pregnant women were enrolled before GA 18 weeks + 6 days. The prevalence of early GDM in the two Danish DALI centers (Copenhagen and Odense combined) was 43% (21). An observational study from the Odense Child Cohort in Denmark among 1,561 pregnant women screened for GDM found a prevalence of GDM at 40% according to WHO 2013 GDM criteria (22). Overall, early GDM prevalence in the DALI study varied from 11 to 43% between centers, suggesting population-specific differences. A recent Dutch study found a WHO 2013 GDM rate of 32% in women with known risk factors for GDM (23).

At baseline, women with WHO 2013 GDM showed higher BMI, glucose, and insulin levels and insulin resistance compared with women with normal glucose tolerance. Other studies have also reported that women with early GDM by WHO 2013 criteria have phenotypic characteristics in common with the metabolic syndrome (24). The UPBEAT study demonstrated that differences in metabolic profile, including exaggerated dyslipidemia, were present at least 10 weeks prior to a diagnosis of GDM in the late second trimester (25). This information may help with identifying women at risk.

At GA 28–30 weeks, LiP women with early GDM by WHO 2013 criteria had higher glucose and insulin levels and lower insulin sensitivity but, paradoxically, lower total cholesterol and LDL levels compared with those without GDM. These findings were not associated with differences in clinical outcomes or GWG, and their clinical and biological significance remains unclear.

A large number of clinical trials in obese pregnant women have been published in recent years as well as three meta-analyses (26–28), with the most recent using individual patient data (IPD) (28). The IPD meta-analysis was based on IPD from >12,000 women obtained from 36 RCTs from different research teams, mainly in Europe, the U.S., and Australia (28). The IPD meta-analysis noted that various interventions based on diet and physical activity during pregnancy reduce GWG. Although there was a trend for active intervention to produce more favorable clinical maternal composite outcomes, statistical significance was not achieved. In consideration of individual maternal outcomes, interventions significantly lowered the risk of cesarean section, and overall effects were consistent across subgroups of women based on ethnicity, parity, age, and BMI. A reason for the limited success of lifestyle intervention trials might be the fact that interventions were initiated relatively late, usually during the second trimester in most studies. Pregnancy may be too advanced and duration of intervention insufficient to overcome the negative impact of a dysmetabolic intrauterine environment in early pregnancy.

To date, most studies on lifestyle intervention in pregnancy have used high prepregnancy BMI as an inclusion criterion and risk factor for macrosomia and GDM. A recent study found that GDM risk among obese women with good adherence to a self-reported healthy diet was similar to risk in a group of normal-weight women (29), indicating that dietary interventions should perhaps be targeted toward women with a low-quality diet instead of focusing on BMI without considering diet. Similarly, for intervention in metabolically ill, rather than healthy, obese women, future studies should consider recruiting participants based on a more comprehensive risk assessment, including hyperglycemia or other metabolic markers in early pregnancy as well as baseline diet and physical activity habits.

Based on our results, lifestyle intervention (without SMBG) in obese women fulfilling WHO 2013 GDM criteria in early pregnancy does not appear to be effective in improving obstetric or metabolic outcomes. Future intervention studies should focus on intervention starting prepregnancy or even much earlier in the life cycle. In addition, awareness of interpregnancy weight management and prevention of excessive GWG should still be important areas of clinical focus to improve maternal and offspring health.

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