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Metabolic syndrome in Finnish women 7 years after a gestational diabetes prevention trial

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ABSTRACT

Background: Risk for developing metabolic syndrome (MeS) after delivery is high among women with gestational diabetes mellitus (GDM), but little is known about development of MeS among women with risk factors for GDM during pregnancy. In the present study, we studied the prevalence of MeS 7 years postpartum among women with GDM risk factors during pregnancy, women with early GDM diagnosis and women without GDM risk factors. We also analysed the early pregnancy risk factors associated with MeS.

Methods: A Finnish cluster randomised controlled GDM prevention trial was conducted in 2007–2009. The prevalence of MeS according to International Diabetes Federation criteria was determined in the follow-up study 7 years after original trial. Eligible participants (n=289) in 4 study groups (intervention (n=83) and usual care (n=87) with GDM risk factors; early GDM (n=51), and healthy control without GDM risk factors (n=68)) were evaluated for MeS. Binary logistic regression models were used to analyse risk factors associated with MeS.

Results: 7 years postpartum, the MeS prevalence was 14% (95% CI 8% to 25%) in the intervention group; 15% (CI 8% to 25%) in the usual care group; 50% (CI 35% to 65%) in the early GDM group and 7% (CI 2% to 18%) in the healthy control group. OR for MeS in women with GDM risk factors did not differ from the healthy control group. Body mass index (BMI)-adjusted OR for MeS was 9.18 (CI 1.82 to 46.20) in the early GDM group compared with the healthy control group. Increased prepregnancy BMI was associated with MeS (OR, 1.17, CI 1.08 to 1.28, adjusted for group).

Conclusions: Increased prepregnancy BMI and early GDM diagnosis were the strongest risk factors for developing MeS 7 years postpartum. Overweight and obese women and especially those with early GDM should be monitored and counselled for cardiometabolic risk factors after delivery.

Strengths and limitations of this study

- Our study was a long-term follow-up of a large gestational diabetes mellitus (GDM) prevention trial.
- The study was one of the first follow-up studies on the prevalence of metabolic syndrome (MeS) after delivery among women with risk factors for GDM.
- The results include data of the MeS prevalence among different risk groups.
- Thirty-seven per cent of the invited women entered the measurements for MeS, and the four subgroups were relatively small.
- The results may have been moderately affected by a healthy selection bias.

INTRODUCTION

Metabolic syndrome (MeS) is a clustering of atherosclerotic risk factors, including abdominal obesity, elevated plasma triglycerides, decreased high density lipoprotein (HDL) cholesterol, elevated blood pressure and elevated fasting glucose.[1 2] Insulin resistance and low-grade inflammation are central drivers in the pathogenesis of MeS.[3 4] In addition to genetic features, obesogenic lifestyle defined by unhealthy diet and physical inactivity increase the risk for MeS.[5–9] The prevalence of MeS is increasing worldwide, along with the obesity epidemic and population ageing.[10 11] Estimates of MeS prevalence vary between 15% and 34% in adult populations,[12–15] and around 8–19% in reproductive-aged women in industrial countries.[16–18] It is relevant to identify patients with MeS, as they are at twice the risk for developing cardiovascular disease over the next 5–10 years, and at fivefold lifetime risk of developing type 2 diabetes compared with individuals without the syndrome.[1]

Gestational diabetes mellitus (GDM) is a disorder in glucose and insulin metabolism first diagnosed during pregnancy.[19] The most important risk factors for GDM are prepregnancy overweight, high maternal age and a family history of type 2 diabetes.[20] Women with a history of GDM are at

increased risk for developing cardiometabolic disorders, such as type 2 diabetes and MeS after delivery.[21 22] MeS and GDM share mutual risk factors, suggesting that women with risk factors for GDM may be at increased risk for future MeS, even in the absence of GDM.[23 24] Overweight and excessive gestational weight gain have been linked to development of GDM and later cardiometabolic disorders.[23 25–27] Long-term follow-up studies on development of MeS among women at increased GDM risk are lacking.

Our cluster randomised controlled trial (RCT) in Finnish pregnant women at increased GDM risk showed that lifestyle counselling was effective in controlling the proportion of large-for-gestational-age new-borns and improving the women's diet, and preventing excessive gestational weight gain and decrease in physical activity.[28–31] One year after delivery, the prevalence of MeS among women with GDM risk factors was 16–18% depending on the criteria; with no differences between the intervention and usual care group.[24]

Our aim is to study MeS and its components 7 years postpartum among Finnish women who in early pregnancy were at increased risk of developing GDM (intervention or usual care), among women with early pregnancy GDM diagnosis and among women without GDM risk factors during pregnancy (healthy control). We also studied risk factors associated with the development of MeS 7 years postpartum.

METHODS

Participants and study design

The study is a 7-year follow-up of a cluster RCT on GDM prevention (ISRCTN33885819). Detailed descriptions of the design and methods of the original study have been published previously.[32] The study was conducted in 14 primary healthcare maternity clinics in Western Finland in 2007–2009, a 1-year postpartum follow-up in 2009–2011 and the 7-year follow-up in 2014–2016.

The primary aim of the trial was to prevent GDM and excessive gestational weight gain among pregnant women with an increased risk for GDM. Maternity clinics were randomised into seven intervention and seven control clinics. Pregnant women were recruited by nurses at their first visit (8–12 weeks' gestation) in maternity clinics. Women were eligible if they had at least one of the following GDM risk factors: age≥40 years, prepregnancy body mass index (BMI) ≥25 kg/m², GDM or any sign of glucose intolerance in any previous pregnancy, a macrosomic baby (≥4500 g) in any previous pregnancy or diabetes in first-degree or second-degree relatives. The main exclusion criteria were age<18 years, a GDM diagnosis at 8–12 weeks' gestation, twin pregnancy, physical restrictions that precluded exercise or a clinical history of chronic disease. A diagnosis of GDM was based on a 2-hour 75 g oral glucose tolerance test (OGTT) according to at least one of the following criteria: fasting plasma glucose of ≥5.3 mmol/L, >10.0 mmol/L at 1 hour or >8.6 mmol/L at 2 hours.[33]

The original intervention included individual counselling on weight gain, diet and physical activity by public health nurses during five routine visits to maternity clinics. The women in the control clinics received usual maternal care, which also included some lifestyle advice.

Of 888 pregnant women who participated in the baseline assessments at 8–12 weeks' gestation, 442 (50%) were eligible for the original study (intervention and usual care group) (figure 1). Further, 374 were excluded, of whom 174 due to a GDM diagnosis at 8–12 weeks' gestation (early GDM group). The healthy control group consisted of 176 women who did not meet the inclusion criteria.

Seven hundred and eighty-eight women were invited to participate in the follow-up study 7 years (mean 7.2, range 5.6–8.3) after delivery, and 289 women participated.

The study was conducted in accordance with the Declaration of Helsinki (2000), and it was approved by Pirkanmaa University Hospital District Ethics (Ref. number R14039). The participants completed a written informed consent before participation.

Laboratory measurements

Information on maternal measurements by the nurses was obtained from the standard maternity cards. Height was measured at the first maternity care visit (8–12 weeks' gestation), and weight was measured at each maternity care visit, and at 1 and 7 years postpartum. Waist circumference was measured at 1 and 7 years postpartum, and the average of three measurements was used in the analysis. Blood pressure was measured in duplicate at each maternity care visit and at 1 and 7 years postpartum.

Blood samples for glucose, cholesterol, HDL cholesterol and triglyceride analysis after a 12-hour fast, and a 2-hour OGTT were collected at baseline and at 1 and 7 years postpartum. All blood analyses were performed at the UKK Institute. During the OGTT, the participants drank 75 g glucose in 330 mL water (Glucodyn, Ultimed, Finland), and the samples were taken after 60 and 120 min. Plasma glucose concentrations were measured fresh within 24 hours after the OGTT. Plasma samples for lipid analysis were stored frozen at −80°C until analysed. Citric acid/fluoride and EDTA tubes were used for glucose and lipid analysis of venous blood. Glucose, total cholesterol, HDL cholesterol and triglyceride concentrations were determined in enzymatic assays using a Roche Cobas Mira Plus analyser. All testing was performed in duplicate.

MeS was diagnosed according to International Diabetes Federation (IDF) criteria.[1] The diagnosis was set if any three of the five criteria were present: increased waist circumference (>80 cm); elevated triglycerides (≥1.7 mmol/L), or specific medication; reduced HDL cholesterol (<1.3 mmol/L), or specific medication, elevated fasting glucose (≥5.6 mmol/L), or specific

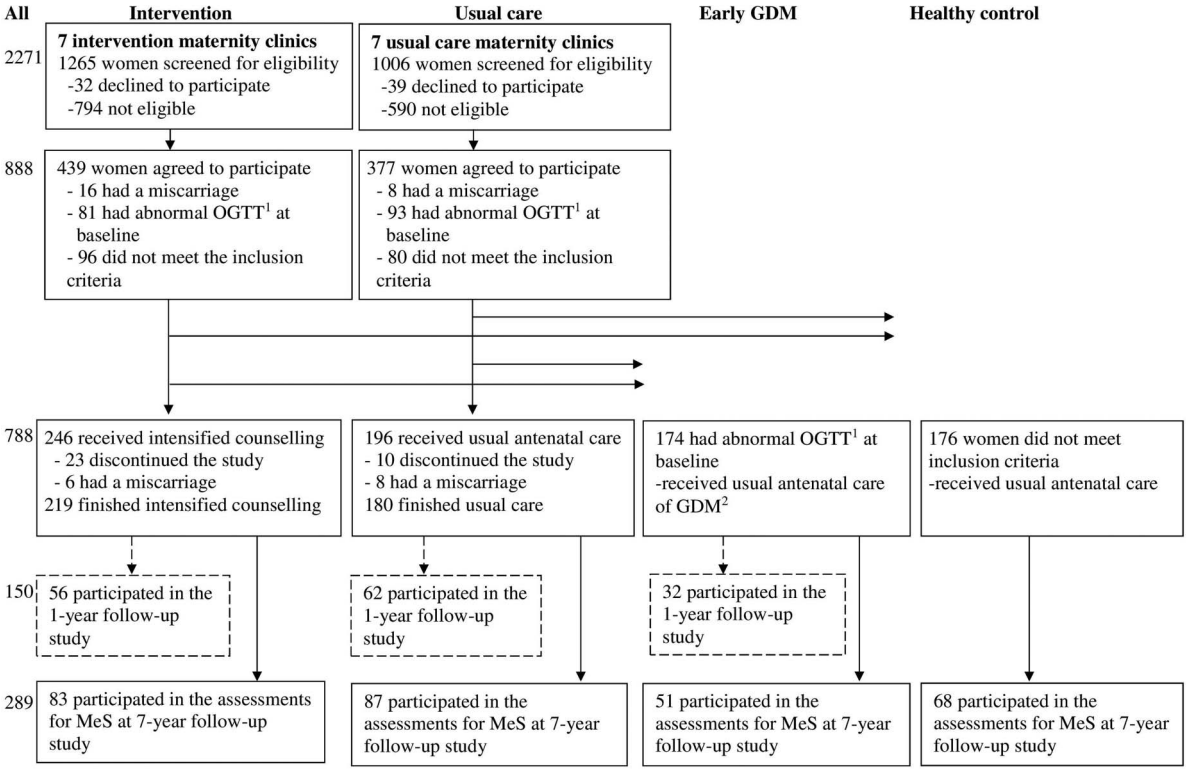

Figure 1 Flow diagram of the study. The two intervention groups (intervention and usual care), early gestational diabetes mellitus and healthy control groups were invited for follow-up measurements 7 years after intervention.

medication, and elevated blood pressure (≥130 or 85 mm Hg), or specific medication.

Statistical analyses

The background characteristics and descriptive information on components and the prevalence of MeS are reported as means and SDs or frequencies and proportions. The Wilson score method without continuity correction was used to calculate 95% CIs for prevalence. A χ^2 test was used to investigate whether distributions of categorical variables differed from one another. Continuous variables were normally distributed. We used one-way analysis of variance to compare means across groups. Differences in continuous variables between the healthy control or the early GDM group compared with the other three groups merged together were tested by independent samples t-test. Binary logistic regression models were used to obtain ORs and their 95% CIs to study associations between MeS and its explanatory variables. Explanatory variables were group (the intervention, the usual care, the early GDM and the healthy control as a reference group), age (continuous), BMI (continuous) and the five GDM risk factors which were used in entrance criteria to the original study: BMI ≥25 kg/m², age≥40 years, GDM or any sign of glucose intolerance in any previous pregnancy, a macrosomic baby (≥4500 g) in any previous pregnancy, and diabetes in first-degree or second-degree relatives. Based on the rule of 10 events per variable, multivariable logistic regression models were adjusted only for BMI and GDM or any sign of glucose intolerance in any previous pregnancy. The results were considered to be statistically significant if p<0.05. All analyses were performed with SPSS software (V.20.0).

RESULTS

Background characteristics

Table 1 shows the characteristics of the 289 women who participated in the follow-up study 7 years postpartum. The mean age of the participants was 37.8 years (range 25–52 years) and the mean number of deliveries was 2.5 (range 1–9). Twenty-nine (10%) women smoked frequently or occasionally. The most common inclusion criteria for the study were prepregnancy overweight or obesity, and diabetes in first-degree or second-degree relatives. Women with early GDM fulfil the inclusion criteria of being overweight (p<0.001) and having a history of GDM (p=0.002) more often than others. Healthy controls did not meet inclusion criteria (GDM risk factors) at baseline. The prevalence of overweight and obesity 7 years postpartum (53%, 69%, 80%) had stayed around the same level, or slightly increased, compared with early pregnancy (48%, 68%, 78%) among women in the intervention, usual care and early GDM group, respectively. Four women (2 in the early GDM and 2 in the healthy control group) had medication for type 2 diabetes. Sixteen (5%) women had medication for dyslipidaemias and eight (3%) for hypertension, with no

Table 1 Background characteristics of women at 7 years postpartum

	Intervention (n=83)	Usual care (n=87)	Early GDM (n=51)	Healthy control (n=68)	All (n=289)
Age (years)	37.7±4.5	38.0±4.9	38.6±4.3	37.0±5.2	37.8±4.8
Weight (kg)	75.6±17.3	76.9±13.1	84.5±16.3	62.9±7.6	74.6±15.7
BMI (kg/m^2)	27.2±5.5	28.1±5.1	30.1±5.6	22.7±2.5	26.9±5.4
BMI 25–29.9 kg/m^2	17 (20)	39 (45)	41 (35)	12 (18)	86 (29)
BMI ≥30 kg/m^2	27 (33)	21 (24)	23 (45)	0 (0)	71 (25)
Smoking					
No	73 (91)	77 (91)	45 (94)	57 (84)	252 (90)
Occasionally or daily	7 (9)	8 (9)	3 (6)	11 (16)	29 (10)
Education					
Basic or secondary education	25 (31)	25 (28)	19 (37)	20 (31)	89 (31)
Polytechnic education	28 (34)	40 (46)	20 (39)	29 (45)	117 (41)
University degree	29 (35)	23 (26)	13 (25)	16 (25)	81 (28)
Parity	2.4±1.0	2.6±1.2	2.6±1.6	2.5±1.0	2.5±1.2
1	8 (10)	12 (14)	6 (13)	6 (9)	32 (12)
2–3	66 (84)	60 (71)	35 (74)	50 (75)	211 (76)
≥4	5 (6)	12 (14)	6 (13)	11 (16)	34 (12)
GDM risk criteria (at 8–12 weeks' pregnancy)					
BMI ≥25 kg/m^2	40 (48)	59 (68)	39 (78)	NA	138 (48)
Macrosomic child in any previous pregnancy	3 (4)	3 (3)	5 (10)	NA	11 (4)
GDM in any previous pregnancy	13 (16)	7 (8)	13 (39)	NA	33 (12)
Diabetes in first-degree or second-degree relatives	53 (64)	43 (49)	25 (50)	NA	121 (42)
Age ≥40 years	3 (4)	5 (6)	0 (0)	NA	8 (3)

Means and SDs or frequencies (and proportions) of participants (n=289). BMI, body mass index; GDM, gestational diabetes mellitus.

difference between groups. Eighty-one (28%) women reported hormonal contraception.

Women with early GDM had higher mean weight (p<0.001) and BMI (p<0.001) compared with women in the other three groups. Significant association between group and overweight (p<0.001) and obesity (p<0.001) was found, so that women with early GDM were more often overweight and obese than women in the other groups. Healthy controls, on the other hand, had lower mean weight (p<0.001) and lower BMI (p<0.001). They were less often overweight or obese compared with women in the other three groups, both of the associations being significant (p<0.001). There were no other between-group differences in the background characteristics. Compared with baseline (at 8–12 weeks' pregnancy), the women had gained weight on average 3.1 kg (SD 7.0, range −33.2 to 25.1 kg). The groups did not differ statistically significantly from each other. The healthy control group seemed to have had gained less weight than the other three groups (1.8 vs 3.5, p=0.13). Twelve (9%) women of the intervention group and seven (5%) women of the usual care group and none of the healthy control group had been diagnosed for GDM at 26–28 weeks' pregnancy.

MeS and its components 7 years postpartum

The prevalence of MeS among all women was 19% (95% CI 15% to 25%) (table 2). Among women with GDM risk factors, the prevalence was 14% (95% CI 9% to 21%), with no difference between the intervention (14%, 95% CI 8% to 25%) and the usual care group (15%, 95% CI 8% to 25%). The prevalence was highest among the early GDM group (50%, 95% CI 35% to 65%) and lowest among the healthy control group (7%, 95% CI 2% to 18%). Two (11%) of the 19 women with the GDM diagnosis at 26–28 weeks' gestation had MeS at 7 years postpartum.

Seventy-two per cent of the women exceeded the waist circumference limit of 80 cm (increased waist circumference) and almost half exceeded the limit of 88 cm (abdominal obesity). HDL was reduced (≤1.3 mmol/L) among half of the women. All women with the MeS diagnosis exceeded the waist circumference of 80 cm. Women in the early GDM group had a larger mean waist circumference (p<0.001), higher fasting glucose (p<0.001), higher systolic blood pressure (p=0.047) and higher TG (p<0.0001). They more often exceeded the limits for increased waist circumference and abdominal obesity (p<0.001 and p=0.002), impaired fasting glucose (p<0.001) and increased TG (p<0.001) compared with the three other groups. Healthy controls had a smaller mean waist circumference (p<0.001), lower systolic (p=0.01) and diastolic (p=0.03) blood pressure and higher HDL (p=0.02), and they less often exceed the limits for increased waist circumference (p<0.001) and decreased HDL (p=0.03) compared with the other

Table 2 Components of metabolic syndrome (MeS) and the prevalence of MeS according to International Diabetes Federation criteria

	Intervention (n=64–74)	Usual care (n=66–78)	Early GDM (n=40–45)	Healthy control (n=44–51)	All (n=217–248)	Missing values (N)*
Waist circumference (cm)*	89.9±13.0	90.9±12.8	97.9±14.6	79.5±6.5	89.5±13.5	0, 3, 0, 0
Waist ≥80 cm	52 (70)	59 (79)	42 (93)	24 (47)	177 (72)	
Waist ≥88 cm	41 (55)	42 (56)	32 (71)	6 (12)	121 (49)	
Fasting glucose (mmol/L)	5.2±0.5	5.2±0.4	5.6±0.5	5.2±0.4	5.3±0.5	5, 12, 3, 6
Fasting glucose ≥5.6 mmol/L or medication	10 (15)	7 (11)	21 (49)	4 (9)	42 (19)	
Systolic pressure (mm Hg)	119±13	118±12	122±11	114±14	118±12	2, 3, 1, 4
Diastolic pressure (mm Hg)	77±10	78±10	79±7	75±10	77±10	2, 3, 1, 4
Blood pressure ≥130 or ≥85 mm Hg or medication	10 (14)	13 (17)	8 (18)	6 (13)	37 (16)	
HDL cholesterol (mmol/L)	1.30±0.27	1.28±0.38	1.28±0.36	1.41±0.30	1.32±0.34	10, 0, 2, 1
HDL cholesterol ≤1.3 mmol/L or medication	33 (52)	41 (53)	25 (58)	18 (36)	117 (50)	
Triglycerides (mmol/L)	0.91±0.34	1.05±0.67	1.36±0.88	0.95±0.38	1.05±0.61	10, 0, 2, 1
Triglycerides ≥1.7 mmol/L	1 (2)	9 (12)	12 (28)	5 (10)	27 (12)	
Metabolic syndrome	9 (14)	10 (15)	20 (50)	3 (7)	42 (19)	10, 7, 5, 7

Means and SDs or frequencies (and proportions) of participants. GDM, gestational diabetes mellitus.
*Number of missing values in the intervention, usual care, early GDM, healthy control groups, respectively.

groups. There were no differences in the components MeS between the intervention and usual care groups.

Fifty-five (27%) women did not meet the criteria for any MeS component: 14 (23%) women in the intervention group, 14 (22%) in the usual care group, 7 (18%) in the early GDM group and 20 (46%) in the healthy control group. Most women (n=115, 56%) met one or two MeS components.

Risk factors of MeS

Univariable binary logistic regression models

In univariable logistic regression models, the OR for developing MeS 7 years postpartum among women with increased GDM risk during pregnancy (intervention and usual care) did not differ statistically significantly from the healthy control group (table 3). OR for MeS among women with early GDM was 21.0 (95% CI 4.47 to 98.7) compared with the healthy controls, and 6.0 (95% CI 2.7 to 13.2) compared with the intervention and the usual care groups (not presented). Prepregnancy BMI (OR 1.20, 95% CI 1.11 to 1.29, p<0.001), prepregnancy overweight or obesity (OR 8.06, 95% CI 3.21 to 20.2, p<0.001) and GDM or any sign of glucose intolerance in any previous pregnancy (OR 3.21, 95% CI 1.34 to 7.69, p<0.01) were associated with increased occurrence of MeS. The other GDM risk factors (macrosomic baby in any previous pregnancy, diabetes in relatives or age) were not associated with the MeS occurrence 7 years postpartum.

Multivariable binary logistic regression models

In a multivariable regression model 1, adjusted for prepregnancy BMI, the OR for developing MeS 7 years postpartum among women with increased GDM risk during pregnancy (intervention and usual care) did not differ significantly from the healthy control group (table 3). Women with early pregnancy GDM had increased odds for MeS compared with the healthy control group (OR 9.18, 95% CI 1.82 to 46.20, p=0.007). Also increased prepregnancy BMI was associated with increased odds for MeS (OR 1.20, 95% CI 1.11 to 1.29, p<0.001). In a multivariable regression model 2, adjusted for BMI and GDM or any sign of glucose intolerance in any previous pregnancy, early GDM when compared with the healthy control group (OR 97.75, 95% CI 1.50 to 40.0, p=0.014), and increased prepregnancy BMI (OR 1.19, 95% CI 1.09 to 1.31, p<0.001) were associated with the MeS occurrence. GDM or any sign of glucose intolerance in any previous pregnancy was not associated with the MeS occurrence 7 years postpartum.

Dropout analyses

Data for 7-year follow-up for MeS were available for 37% of the women who were invited to participate after 7 years (n=788). Of the women invited to follow-up study, 17% were not willing to participate, 26% were out of reach and 20% only completed a follow-up questionnaire. Dropout analyses showed that the women participating the 7-year follow-up study were older at the baseline (30.2 vs 29.2, p<0.01), were less often frequent or occasional smokers before pregnancy (17% vs 30%, p<0.001) and were higher educated (university degree 28% vs 19%, p<0.009) compared with the non-participants. There were no differences between the groups in other background characteristic (BMI, parity

Table 3 Logistic regression models with ORs and 95% CIs and p values (n=217) for occurrence of metabolic syndrome (according to International Diabetes Federation criteria) by its explanatory variables (group, age, body mass index and five gestational diabetes mellitus risk factors)

	Univariable logistic regression models		Multivariable logistic regression model 1		Multivariable logistic regression model 2	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Group (reference=healthy control)						
Intervention	3.44 (0. 71 to 16.8)	0.13	1.64 (0.31 to 8.79)	0.56	1.29 (0.23 to 7.18)	0.77
Usual care	3.15 (0.65 to 15.3)	0.16	1.39 (0.26 to 7.41)	0.70	1.17 (0.21 to 6.41)	0.85
Early GDM	21.0 (4.47 to 98.7)	<0.001	9.18 (1.82 to 46.20)	0.007	7.75 (1.50 to 40.0)	0.014
Age (early pregnancy, continuous)	1.07 (1.00 to 1.15)	0.052				
BMI (prepregnancy, continuous)	1.20 (1.11 to 1.29)	<0.001	1.17 (1.08 to 1.28)	<0.001	1.19 (1.09 to 1.31)	<0.001
GDM risk factors during early pregnancy						
BMI ≥25 kg/m^2 (prepregnancy)	8.06 (3.21 to 20.2)	<0.001				
A macrosomic baby (≥4500 g) in any previous pregnancy	0.74 (0.09 to 6.34)	0.78				
GDM or any sign of glucose intolerance in any previous pregnancy	3.21 (1.34 to 7.69)	<0.01			2.07 (0.74 to 5.78)	0.17
Type 1 or 2 diabetes in first-degree or second-degree relatives	1.04 (0.52 to 2.09)	0.91				
Age ≥40 years	0.74 (0.09 to 6.34)	0.78				

GDM, gestational diabetes; BMI, body mass index.
Univariable logistic regression models: separate models for each explanatory variables without adjustments.
Multivariable logistic regression model 1: adjusted for one explanatory variable (BMI).
Multivariable logistic regression model 2: adjusted for two explanatory variables (BMI, and GDM or any sign of glucose intolerance in any previous pregnancy).

or GDM risk criteria), laboratory measurements or group distribution.

DISCUSSION

Seven years postpartum, MeS was diagnosed among 14% (95% CI 9% to 21%) of the women with risk factors for GDM during pregnancy. The MeS prevalence was highest among women with a diagnosis of early GDM (50%, 95% CI 35% to 65%), and lowest among the healthy control group (7%, 95% CI 2% to 18%). Diagnosis of early GDM and increased prepregnancy BMI were the strongest risk factors for developing MeS. Prepregnancy and present overweight or obesity were common among women with GDM risk factors, and especially among those with early GDM.

In a prospective Finnish population study among women aged 36 and 39, the MeS prevalence was 18% and 23% according to the IDF definition.[18] Compared with these levels, the MeS prevalence in our study was somewhat lower among women with an increased risk for GDM. Therefore, increased GDM risk seemed not to be associated with a higher MeS prevalence 7 years postpartum. Compared with the women aged 35–45 and 25–60 years in a Finnish population study in 2012, however, the women with increased GDM risk were more often obese (28% vs 16%),[34] and abdominally obese (waist circumference >88 cm) (56% vs 30%).[35] These differences are relevant, as especially abdominal obesity is the most important independent factor in the development of MeS.[10] The finding may indicate future risk in our participants. Overweight was also the most common inclusion criteria (GDM risk criteria) in our study, which apparently had an influence on the high prevalence of overweight and obesity postpartum.

However, the intervention (14%, 95% CI 8% to 25%) and usual care (15%, 95% CI 8% to 25%) group did not differ from each other in the prevalence of MeS or its components after 7 years, even though counselling had positive effects on women's weight gain and lifestyle during pregnancy.[28–31] However, 7 years are a long time, and several factors have affected women's lifestyle. Mothers with small children may have had lack of time and may have got tired to follow the recommended lifestyle habits which were discussed during the intervention. Further, participation in a GDM prevention study may have improved health consciousness and lifestyle habits in the intervention and the usual care group. Additionally, also usual care includes some lifestyle counselling in Finland. Dropout rate was rather high, but since it was non-differential for group, the possibility for bias in the differences between groups remains low.

Our subgroups differed in the prevalence of MeS. Women in the early GDM and women in the healthy control groups represented the extremes (50% vs 7%). Earlier studies have found that history of GDM is strongly associated with a higher risk of future MeS and other cardiometabolic disorders.[36 37] In a Finnish

cohort among 240 women, the risk of developing MeS 2–6 years after pregnancy complicated by GDM was 2.4-fold higher compared with normal pregnancy.[21] In our earlier report of the same original trial, the MeS prevalence among women with early GDM was already elevated (31%) at 1-year postpartum compared with the intervention group (11%).[24] Seven years postpartum, the MeS prevalence among women with early GDM had increased to 50%. Further, women with early GDM had increased odds for MeS compared with other three groups (intervention, usual care and healthy controls). The association remained after adjustment for BMI. Also history of GDM was associated with the MeS occurrence. These findings attest the later cardiometabolic risk associated with GDM. Nevertheless, GDM diagnosis at 26–28 weeks' gestation among the 19 women in the intervention and usual care group seemed not to be associated with higher MeS prevalence in our data. Therefore, our study suggests that GDM was associated with an increased MeS prevalence 7 years postpartum if it was diagnosed in early pregnancy (8–12 weeks). Women with early GDM are a special high risk group for later cardiometabolic disorders. A large meta-analysis found that women with early pregnancy GDM were at a twofold risk for future type 2 diabetes compared with women with later GDM.[26]

Several cardiometabolic risk factors were clustered in the women in the early GDM group. In early pregnancy, they had been more often overweight or obese, and 7 years postpartum, they still were more often overweight or obese, and had components of MeS more frequently than the other women. Further, compared with Finnish female population, the women with early GDM in our study were three times more often obese (45% vs 16%),[34] and over two times more often abdominally obese (waist circumference >88cm) (71% vs 30%).[35] Present obesity partly explains the increased MeS prevalence. Clustering of lifestyle-related risk factors is common.[38–40] Pregnancy-related weight retention tends to be highest among those women who have been overweight or obese before pregnancy.[41 42] Further, many women retain weight after pregnancy, and the mean weight gain associated with parity is around 0.5–3.2 kg, with a high personal variation.[39 43 44] In a Finnish population study, parity-related weight retention was associated with visceral obesity.[45]

High prevalence of obesity promoting insulin resistance was probably the common denominator for the increased prevalence of early pregnancy GDM and MeS after 7 years.[46 47] This finding clearly underlines that it is particularly important to invest in lifestyle counselling among overweight and obese pregnant women entering maternity care. Prevention of excessive weight gain during pregnancy and promoting postpartum weight reduction by individually tailored lifestyle modifications have been effective against weight retention, and in preventing further cardiometabolic disorders, such as MeS in parous women.[48–52] A weight reduction of 5–10% is associated with significant decreases in cardiometabolic risk factors.[53 54] The possibilities for reaching pregnant women in many countries are good due to maternity care systems, but there is often lack of long-term follow-up as the healthcare providers change.[55] Actions to increase cooperation between different providers are needed.

Healthy controls were healthier than the other three groups with GDM risk factors, as assessed by components and the prevalence of MeS at 7 years postpartum. Also compared with the Finnish population, they represented an unexceptionally healthy group, in what comes to the prevalence of obesity (0% vs 16%), abdominal obesity (12% vs 30%) as well as MeS (7% vs 17–23%).[34 35] The results suggest that keeping normal weight and prevention of excessive pregnancy-related weight retention are important in not only preventing GDM, but also in preventing later MeS.

Strengths and limitations

Our study has several strengths. It was a long-term follow-up, from early pregnancy until 7 years postpartum. It was also one of the first follow-up studies of gestational trials, in which the prevalence of MeS has been determined among women with risk factors for GDM. To the best of our knowledge, the only previous follow-up report was ours on the MeS prevalence among women with GDM risk factors at 1-year postpartum.[24] In general, there is a limited amount of studies of the MeS prevalence among reproductive-aged female populations, even though obesity is rapidly increasing worldwide, especially among young adults.[11 56] Our study results include data of the MeS prevalence among different risk groups—women with an increased GDM risk, women diagnosed with early GDM and healthy pregnant women. Also associations between risk factors assessed in early pregnancy and MeS 7 years postpartum have not been identified earlier. Our original trial[32] was one of the largest RCTs about preventing the development of GDM in women with GDM risk factors.

After 7 years, the recruitment of the women of the original study was difficult, and eventually, 37% of the invited women entered the measurements for analyses of MeS. Thirty-seven per cent were either not willing to participate or only completed the follow-up questionnaire. Dropout analyses showed that the results may have been affected by a healthy selection bias, as the women who participated in the follow-up study were less often smokers and were higher educated. On the other hand, the bias affected all four subgroups entering the follow-up study, as they did not differ from each other regarding to the participation rate. The subgroups were relatively small, which weakened the power to compare the subgroups. The study was implemented among Finnish women, and thus, the results can only be generalised to Caucasian populations.

CONCLUSIONS

Seven years postpartum, MeS was diagnosed among 14% of the women with risk factors for GDM during pregnancy, which is less than average. The MeS prevalence was the highest among women with a diagnosis of early GDM (50%), and the lowest among the healthy control group (7%). Early GDM diagnosis and increased prepregnancy BMI were the strongest risk factors for developing MeS. Prepregnancy and present overweight or obesity were common among women with GDM risk factors, and especially among those with early GDM. Overweight and obese women and especially those with early GDM should be monitored and counselled for cardiometabolic risk factors after delivery. Prevention of pregnancy-related weight retention, including excessive gestational and postpartum weight gain, is important for the prevention of MeS. Overweight and obesity among reproductive-aged women is increasing, which represents even a greater challenge in monitoring and managing risk factors for chronic diseases. Larger population studies on the MeS prevalence and evaluation of prevention strategies are needed among reproductive-aged women, especially among those with GDM risk factors.

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Contributors RL, JP, PK, PT and PH initiated the study design; JR and JP performed statistical analyses; JP wrote the paper. All authors contributed to refinement of the study protocol and approved the final manuscript. JP and RL have the primary responsibility for the final content.

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