Received: 2 May 2024 | Accepted: 7 August 2024

DOI: 10.1111/jog.16059

REVIEW ARTICLE

Gestational diabetes mellitus management according to ultrasound fetal growth versus strict glycemic treatment in singleton pregnancies: A systematic review and meta-analysis of clinical trials

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Abstract

Aim: The objective of this meta-analysis was to evaluate obstetric outcomes in gestational diabetes mellitus (GDM) patients treated with flexible management based on intrauterine ultrasound fetal growth (FMIUFG) or strict maternal glycemic adjustment (SMGA).

Methods: We performed a comprehensive systematic review of electronic databases for randomized clinical trials (RCTs) comparing obstetrics outcomes of singleton GDM patients managed according to FMIUFG or SMGA. The review protocol was registered in PROSPERO (CRD497888). Searches were conducted in PubMed, Embase, Cochrane, and LILACS. Primary outcomes were gestational age at delivery and birth weight. Random-effect model meta-analyses were used to minimize the effects of uncertainty associated with inter-study variability. Results are reported as standardized mean differences (SMDs) or as odds ratios (ORs) and their 95% confidence interval (CI). Heterogeneity between studies was estimated using the I^2 statistic. The Cochrane Risk of Bias Scale was used to assess the quality of studies. There were five RCTs with low to moderate risk of bias, including 450 patients managed according to the FMIUFSG and 381 according to the SMGA.

Results: The macrosomia (birthweight >4000 g) rate was lower in pregnancies managed according to FMIUFG than SMGA adjustments (OR: 0.34; 95%CI: 0.16, 0.71). There were no significant differences in hypertensive disorder, cesarean section, neonatal intensive care unit admission, and large newborn for gestational age rates.

Conclusions: The macrosomia rate was lower in women managed with the FMIUFG. There were no significant differences in other obstetric and neonate outcomes.

KEYWORDS
birth weight, fetal growth, gestational diabetes mellitus, macrosomia, maternal glycemic parameters, ultrasound fetal growth

INTRODUCTION

Gestational diabetes mellitus (GDM) is the most prevalent complication among pregnant women. It is related to maternal hyperglycemia, insulin resistance, body mass index (BMI), and higher glucose passage through the placenta into the fetal circulation. Both the mother and the child are at risk of a wide variety of negative clinical consequences, including preeclampsia, metabolic complications, macrosomia, increased risk of cesarean delivery, and neonatal complications.[1] The GDM diagnosis is preceded by excessive fetal growth between 20 and 28 weeks of gestation, and maternal obesity has an additive fetal effect[2,3] Fetuses at 12–16 weeks of gestation in women who later developed GDM were smaller and grew faster from 24 weeks until delivery time as compared to fetuses

from normoglycemic mothers.[3,4] Several authors have reported the use of fetal ultrasound to study GDM pregnancies at risk of metabolic complications, and the early identification of fetal overgrowth or macrosomia.[5,6]

The main treatment of GDM goal is to neutralize those changes and the fetal hyperglycemia related to the higher glucose passage through the placenta into the fetal circulation. Conventional management of GDM is associated with persistence until delivery of fetal abdominal obesity is detected at 24–28 weeks of pregnancy.[7] In addition, the hypertensive disorders of pregnancy, macrosomia risk, and dystocia rates are related to maternal plasma fasting glucose.[8,9] On the contrary, there is evidence that GDM is not a significant risk of macrosomia in women with intensive diabetic treatment.[10] Therefore, some evidence supports the management of GDM based on ultrasound fetal growth rather than the conventional management to neutralize glucose metabolism alterations.[11] A previous meta-analysis of two articles demonstrated that ultrasound-guided management was associated with increase in insulin dose treatment.[12] The present systematic review and meta-analysis report the available evidence concerning fetal development, pregnancy evolution, and risks in GDM patients followed up according to flexible management based on intrauterine ultrasound fetal growth (FMIUFG) or a strict maternal glycemic adjustment (SMGA).

METHODS

Protocol, data sources, and search strategy

This systematic review and meta-analysis of randomized clinical trials (RCTs) followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis Guidelines.[13] The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO-University of York CRD 497888). Studies published in English, French, Portuguese, German, and Spanish were considered for inclusion in this review without restriction. A literature search of electronic databases was performed on PubMed, Embase, Cochrane, and LILACS (Literatura Latino Americana e do Caribe em Ciencias da Saúde) via specific strategies using the keywords "treatment," "therapy," "intervention," "gestational diabetes," "GDM," "prenatal ultrasonography," "fetal ultrasound," "fetus echography," "blood glucose," "glycemic control," and "hyperglycemia" up to December 20, 2023, based on internationally established GDM criteria (Table S1, Supporting Information). References from selected articles were also screened, seeking additional potential publications not captured by the electronic database searches. We also hand-searched the reference lists of articles identified, looking for additional papers. Articles were excluded if they were narrative reviews, abstracts, and conference proceedings, lacked results with validated methods, or were non-human studies. All disagreements regarding inclusion/exclusion were discussed and solved by consensus with all authors.

Study selection, data extraction, and quality assessment

To assess the association between exposures and outcomes we defined the population, exposure, comparator, outcomes, and study design criteria were developed a priori to guide the scope of the review, along with the procedure, selection, and synthesis of the literature search studies were eligible if they met the following inclusion criteria: *Population*: pregnant women with GDM diagnoses reached by validated international scientific criteria or other internationally recognized scientific organizations, without pregestational or obstetric pathology not receiving any treatment. *Exposure*: GDM flexible management according to ultrasound fetal growth. *Comparator*: GDM strict management according to maternal glycemic treatment. *Outcomes*: primary outcomes were gestational age at delivery and birth weight. Secondary outcomes were other maternal and newborn outcomes related to GDM. *Study design*: randomized clinical trials (RCTs) including pregnant women with GDM, without any other obstetric pathology, managed strict management according to ultrasound fetal growth versus strict maternal glycemic treatment of GDM.

The quality of the selected articles was independently assessed by two researchers, in a blinded fashion with the Cochrane Collaboration Risk of Bias tool for RCTs.[14] The following items were evaluated: generation of the allocation sequence, concealment of the allocation sequence, blinding of participants and personnel to outcome assessment, incomplete outcome data, selective outcome, and other biases. For each RCT, each scale item was described as having a low, moderate, high, or unclear risk of bias (Table S3).

Statistical analyses and publication bias

Because studies might have potential differences in phenotype baseline characteristics, recruitment procedures, lifestyle differences, and laboratory measurement differences, we followed the DerSimonian and Laird random-effect model.[15] Continuous outcomes were reported as standardized mean difference (SMD) and standard deviation (SD). Events were expressed as odds ratio (OR) and their 95% confidence intervals (CIs). The Hedges' g method was used to measure effect sizes, interpreting the magnitude of SMDs as small (0.20), moderate (0.50), or large (0.80).[16]

We planned to evaluate statistical heterogeneity using the chi^2, the I^2 statistic, and the between-study variance using the Tau^2. An I^2 value of 0%–30% defined low

heterogeneity, 30%–65% moderate heterogeneity, and >65% substantial heterogeneity.[17] A $p < 0.1$ for the chi^2 and a Tau^2 >1 defined the presence of statistical heterogeneity. One-study leave-out sensitivity analysis was performed to test the robustness of the overall results.[18] Potential publication bias will be estimated if there are enough studies by Begg's funnel plot and Egger's linear regression test if enough studies are available.[19] Statistical analyses were performed using the Review Manager (RevMan 5.3; Cochrane Collaboration, Oxford, UK).

RESULTS

A total of 399 studies were retrieved from databases. After deleting duplicates and screening titles and abstracts, 40 items were identified for abstract evaluation. Twenty-one articles were excluded due to the lack of a control group, five were narrative reviews, and two were unrelated research topics. Finally, five articles were considered for qualitative and quantitative synthesis (Figure 1, Table 1).[20–24] Meta-analyzed studies were performed in Italy,[20] the United States,[21,23] Spain,[22] and Germany.[24] Table 1 displays detailed information on the study periods, location, number of participants, age, gestational age, inclusion or exclusion criteria, study aims, and main GDM results. Further details are displayed in Table S2, including the exclusion criteria and main results of the five meta-analyzed studies. The risk of bias assessment is shown in Table S3: four studies have a low risk of bias,[21–25] and one study has a moderate risk of bias.[22]

Figure 2 and Table 2 display SMD results of forest plots according to FMIUFG and SMGA managements without significant differences between the two approaches for (A) gestational age at delivery (Figure 2a), maternal BMI (Figure 2b), maternal weight gain (Figure 2c), maternal age (Figure 2d), maternal fasting glucose (Figure 2e), and (E) maternal glycosylated hemoglobin (Figure 2f). Figure 3 and Table 2 display

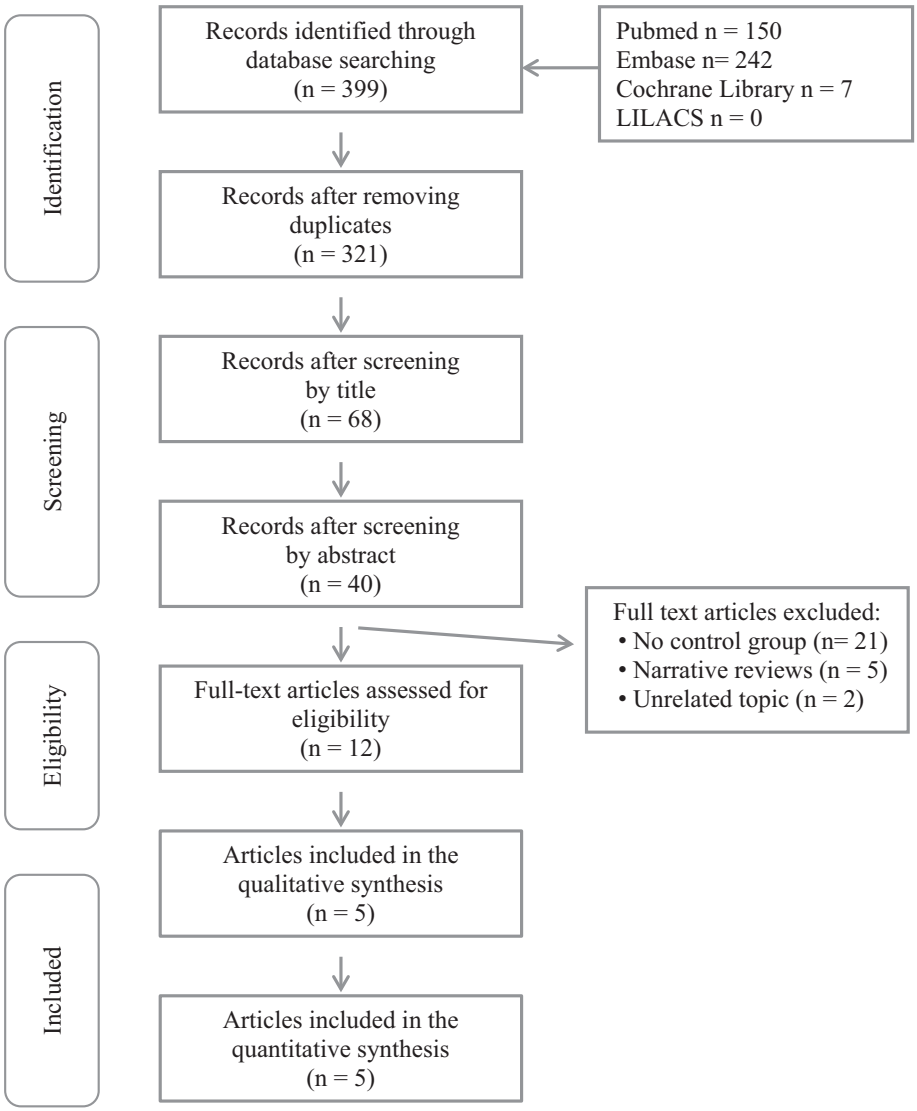


FIGURE 1 Flowchart of study selection.

TABLE 1 Characteristics of randomized controlled clinical trials of singleton pregnancies in women with gestational diabetes mellitus, comparing FMIUFG versus SMGA managements.

Authors	Location and period of study (PoS)	Sample size and age of patients	Inclusion criteria (IC) or reason for exclusion (EC)	Study aims	Gestational age at screening. Maternal glycosylated hemoglobin (HbA1c)	Main results
Bonomo et al.[20]	Milano, Italy. PoS: not reported	USFGF: $n = 151$; age = 33.8 ± 4.6. SMG: $n = 78$; age = 33.5 ± 4.2	IC: pregnant women with GDM diagnosed between 24 and 28 weeks of gestation, without other complications. Ultrasound fetal biometry every 2 weeks from 34 to 38 weeks of pregnancy in the USFGF group.	To study obstetric outcomes in patients with GDM, assigned to a treatment protocol providing different glucose targets in the function of the ultrasound measurement of insulin-sensitive fetal tissues.	Between 24 and 28 weeks of gestation. HbA1c: USFGF: 2.05 ± 0.2; SMGA: 2.05 ± 0.2	Pregnancy outcome was better in ultrasound-modified treatment with a lower rate of large for age gestational (7.9% vs. 17.9%), small for age gestational (6.0% vs. 9.0%), and macrosomia (3.3% vs. 11.5%).
Buchanan et al.[21]	Los Angeles, USA. PoS: October 1989 through March 1992	USFGF: $n = 29$; age = 32.4 ± 5.4 SMG: $n = 30$, age 30.03 ± 5.9	IC: Women with GMD and fetal abdominal circumference >75th percentile.	To test whether fetal growth parameters could be used to identify pregnancies at risk for fetal overgrowth and whether intensive insulin treatment could reduce that risk.	Between 29 and 33 weeks gestation. HbA1c: not reported	Fetal ultrasound early in the third trimester identified women with mild GDM. Insulin treatment reduced the macrosomia risk, indicating that fetal ultrasound can be used to guide metabolic therapy in pregnancies complicated by mild GDM
Fernández-López et al.[22]	Murcia, Spain. PoS: February 2017 through March 2019	USFGF: $n = 121$, age 34.06 ± 4.74; SMG: $n = 125$, age 33.47 ± 4.73	IC: Maternal age of ≥18 years, singleton pregnancy, and GDM diagnosis before <34 weeks.	To compare conventional GDM treatment to flexible treatment based on the measurement of fetal abdominal circumference	Gestational age <34 weeks. USFGF: 29.26 ± 2.8 weeks, HbA1c: 5.16 ± 0.43; SMGA: 29.31 ± 2.74 weeks, HbA1c: 5.18 ± 0.38	The treatment of flexible GDM according to the measurement of fetal abdominal circumference is safe for the mother and the fetus.
Kjos et al.[23]	Los Angeles, USA. PoS: October 1995 through November 1997.	USFGF: $n = 49$ patients; SMG: $n = 49$ patients. Age: no reported.	IC: Gestational age >34 weeks at the time of study entry. EC: multiple pregnancy; medical complications (e.g., hypertension or vascular disease, except GDM); no estimation of gestational age, first clinical exam >20 weeks; use of tobacco, alcohol, or illicit drugs during pregnancy.	This study combined higher glycemic thresholds to initiate insulin therapy, with monthly ultrasound assessments of fetal growth. Pregnancies that continued to have a low risk for macrosomia (normal fetal abdominal circumference) were permitted more relaxed glycemic targets. Pregnancies with a greater risk of macrosomia initiated intensive insulin therapy with titration to achieve strict euglycemic control	Gestational age >14 and <34 weeks. USFGF: 26.96 ± 6.2 weeks, HbA1c 6.4 ± 0.83; SMGA: 26.9 ± 6.2 weeks; HbA1c: 6.8 ± 1.2 and diagnosis diabetes: USFGF: 20.6 ± 7.4; SMGA: 0.7 ± 7.5	In women with GDM and fasting hyperglycemia, glucose plus fetal abdominal circumference measurements identified pregnancies at low risk for macrosomia and resulted in the avoidance of insulin therapy in 38% of patients without increasing rates of neonatal morbidity.

TABLE 1 (Continued)

Authors	Location and period of study (PoS)	Sample size and age of patients	Inclusion criteria (IC) or reason for exclusion (EC)	Study aims	Gestational age at screening. Maternal glycosylated hemoglobin (HbA1c)	Main results
Schaefer-Graf et al.[24]	Berlin, Germany. PoS: January 2000 through January 2003.	USFGF: $n = 100$; SMGA: 99 patients. Age not reported.	EC: Multiple pregnancy, gestational age >34 weeks, maternal medical complications; abuse of tobacco, alcohol, or illicit drugs during pregnancy	To compare management based solely on strict glycemic criteria with a strategy based predominantly on fetal abdominal growth in Caucasian women with GDM	Gestational age 16–34 completed weeks: USFGF: 26.2 ± 4.3 weeks and entry in 29.1 ± 3.4 weeks; HbA1c: 5.2 ± 1.0. SMGA: 26.1 ± 4.3 weeks at diagnosis, 29.0 ± 3.8 at entry. HbA1c: 5.1 ± 0.6	GDM management predominantly based on USFGF resulted in a treatment assignment in 34% of women that would have been different had a maternal glycemia-only strategy been applied. The inclusion of ultrasound fetal growth provides the opportunity to reduce glucose testing in GDM low-risk pregnancies.

neonatal outcomes of the two management options (FMIUFG vs. SMGA) which were not significant for birthweight (Figure 3a), newborn length (Figure 3b), and newborn abdominal circumference (Figure 3c).

Figure 4 and Table 2 display the risks of obstetric and neonatal events. There were no significant differences between the FMIUFG versus SMGA management options for maternal hypertensive disorders of pregnancy (Figure 4a), cesarean section rate (Figure 4b), (C) neonatal hypoglycemia rate (Figure 4c), or (D) transfer to the Neonatal Intensive Care Unit (Figure 4d). The risk of macrosomia (birthweight >4000 g) was lower in patients managed according to ultrasound fetal growth compared to management according to maternal glycemic control (Figure 4e, Hedges' g moderate).

The results of a one-study-leave-out sensitive analysis for birth weight are robust, without significant changes as a representation of fetal global outcome (Table 3). There were no options to design a funnel plot analysis with Begg's correlation and Egger's regression tests or subgroup analyses since the few available studies.

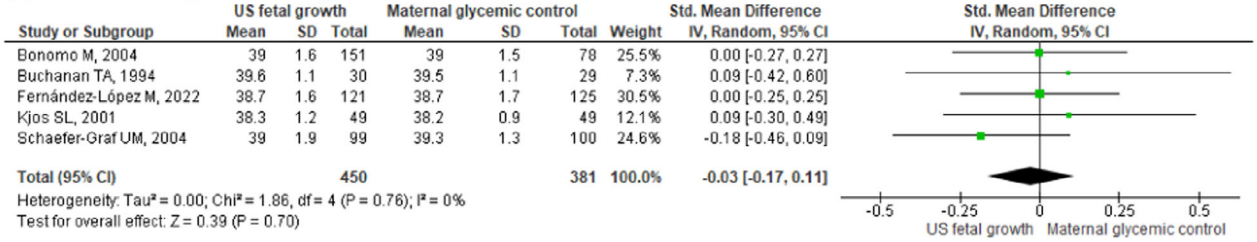
DISCUSSION

Main findings and interpretation

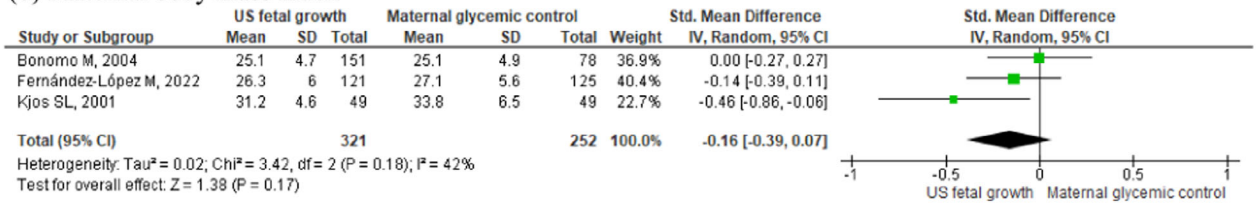
This systematic review and meta-analysis demonstrated that FMIUFG versus SMGA management options reported similar quantitative outcomes in maternal and fetal continuous outcomes. In addition, the macrosomia risk (neonatal weight ≥4000 g) was significantly lower in patients following the fetal ultrasound growth assessment management compared to those following the strict glycemic option. Other categorical variables were not significantly different in both types of management. Ultrasound exam is an essential technique for the evaluation of pregnancy, clinical evolution, GDM risks, and related adverse events. Ultrasound pregnancy exam allows us to assess the clinical evolution and to determine the fetal weight and liver volume[25,26] which are predictors of GDM macrosomia.[27] This finding suggests that fetal ultrasound provides earlier evidence of the macrosomia risk, suggesting the early fetal lability to undetected changes despite the appropriate GDM treatment according to maternal glucose metabolism. Fortunately, ultrasound exams of fetal growth are currently a common clinical practice to identify excessive fetal growth and health status.[28]

GDM is a frequent complication of pregnancy whose prevalence is high and increasing among women with a later age of pregnancy, multiparity, cesarean delivery rate, excessive body weight, previous history of GDM, family history of diabetes, ethnicity, and low physical activity.[29,30] Diagnosis is usually performed during the second trimester of pregnancy, although metabolic glucose dysfunction is present before the conventional period of its diagnosis.[30,31] At 22–24 weeks of gestation, some 3 weeks before the GDM metabolic diagnosis, fetuses display lower head circumference, femur length, and fetal weight, being the findings among parous pregnant women.[32] From 24 weeks of pregnancy, the fetal size is progressively greater in GDM patients compared to those without the endocrine disorder,[4] and there is a positive association between increasing maternal glucose levels with macrosomia, preeclampsia, incidence of cesarean section, macrosomia, shoulder dystocia, primary

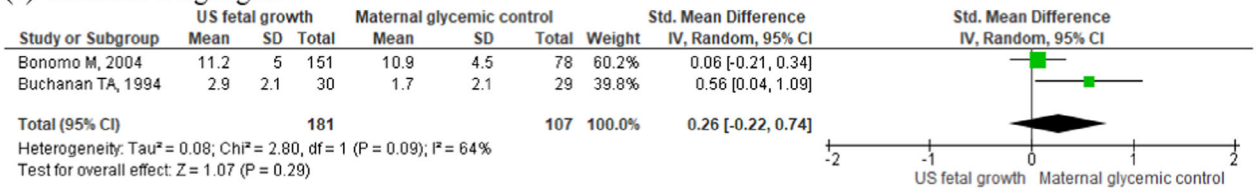
(a) Gestational age at delivery



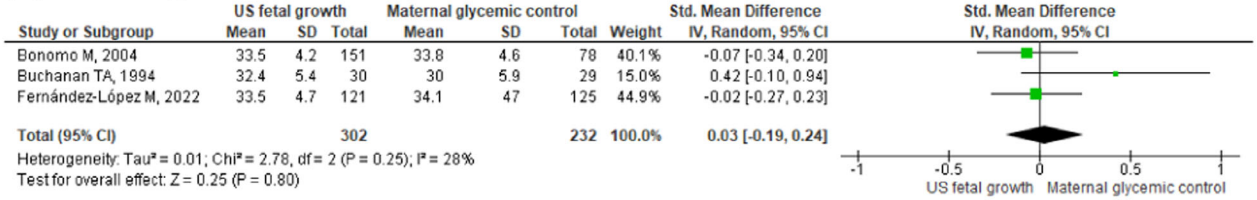
(b) Maternal body mass index



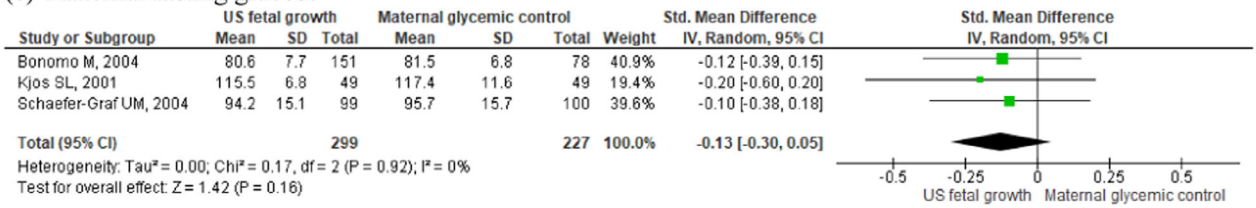
(c) Maternal weight gain



(d) Maternal age



(e) Maternal fasting glucose



(f) Maternal glycosylated hemoglobin

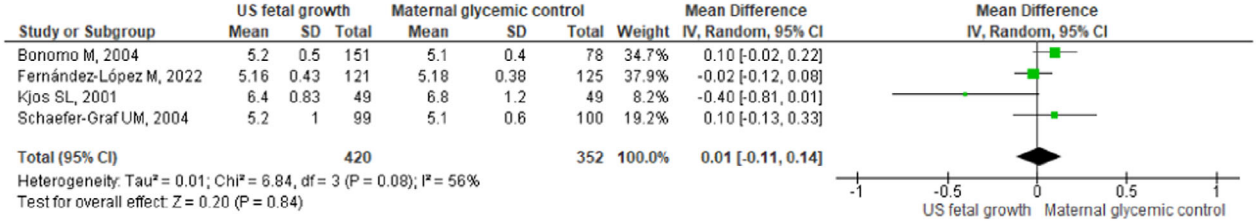


FIGURE 2 Forest plots of studies comparing (a) gestational age at delivery, (b) maternal weight gain, (c) maternal body mass index, (d) maternal age, (e) maternal fasting glucose, and (f) maternal glycosylated hemoglobin in pregnant women with gestational diabetes mellitus managed according to ultrasound fetal growth or maternal glycemic control.

TABLE 2 Meta-analyses of outcomes, involved studies, subjects according to FMIUFG and SMGA, standardized mean differences (SMD) and 95% confidence interval (C.I.), *Z* scores (*p* values for comparisons), and heterogeneity (I^2) for maternal and newborn outcomes.

Outcomes	Involved studies	Subjects (*n*): FMIUFG/SMGA	SMD (95% C.I.)	*Z* score (*p*)	I^2 (%)
Gestational age at delivery	5	450/381	−0.03 (−017, 0.11)	0.39 (0.70)	0
Maternal body mass index	3	321/252	0.6 (−0.39, 0.07)	1.38 (0.17)	42
Maternal weight gain	2	181/107	0.26 (−0.22, 0.74)	1.07 (0.29)	64
Maternal age	3	302/232	0.03 (−0.19, 0.24)	0.25 (0.80)	28
Maternal fasting glucose	3	299/227	−0.13 (−0.30, 0.05)	1.42 (0.16)	0
Maternal glycosylated hemoglobin	4	420/352	0.01 (−0.11,0.14)	0.20 (0.84)	58
Birthweight	5	450/381	−0.11 (−0.30, 0.07)	1.19 (0.23)	39
Newborn length	3	230/156	0.13 (−0.42, 0.15)	0.91 (0.38)	42
Newborn abdominal circumference	2	272/203	0.17 (−5.00, 5.35)	0.02 (0.95)	25
Hypertensive disorders of pregnancy	4	401/332	0.78 (0.56, 1.08)	1.49 (0.14)	0
Cesarean section rate	4	401/332	0.78; (0.56, 1.08)	1.49 (0.14)	0
Neonatal hypoglycemia	2	272/203	1.00 (0.42, 2.39)	0 (1)	0
Transfer to the neonatal intensive care unit	4	419/351	0.85 (0.51, 1.40)	0.63 (0.53)	0
Newborn large for gestational age	5	449/380	0.65 (0.33, 1.28)	1.23 (0.22)	53
Birthweight >4000 g	4	350/280	0.34 (0.16, 0.71)	2.86 (0.004)	17

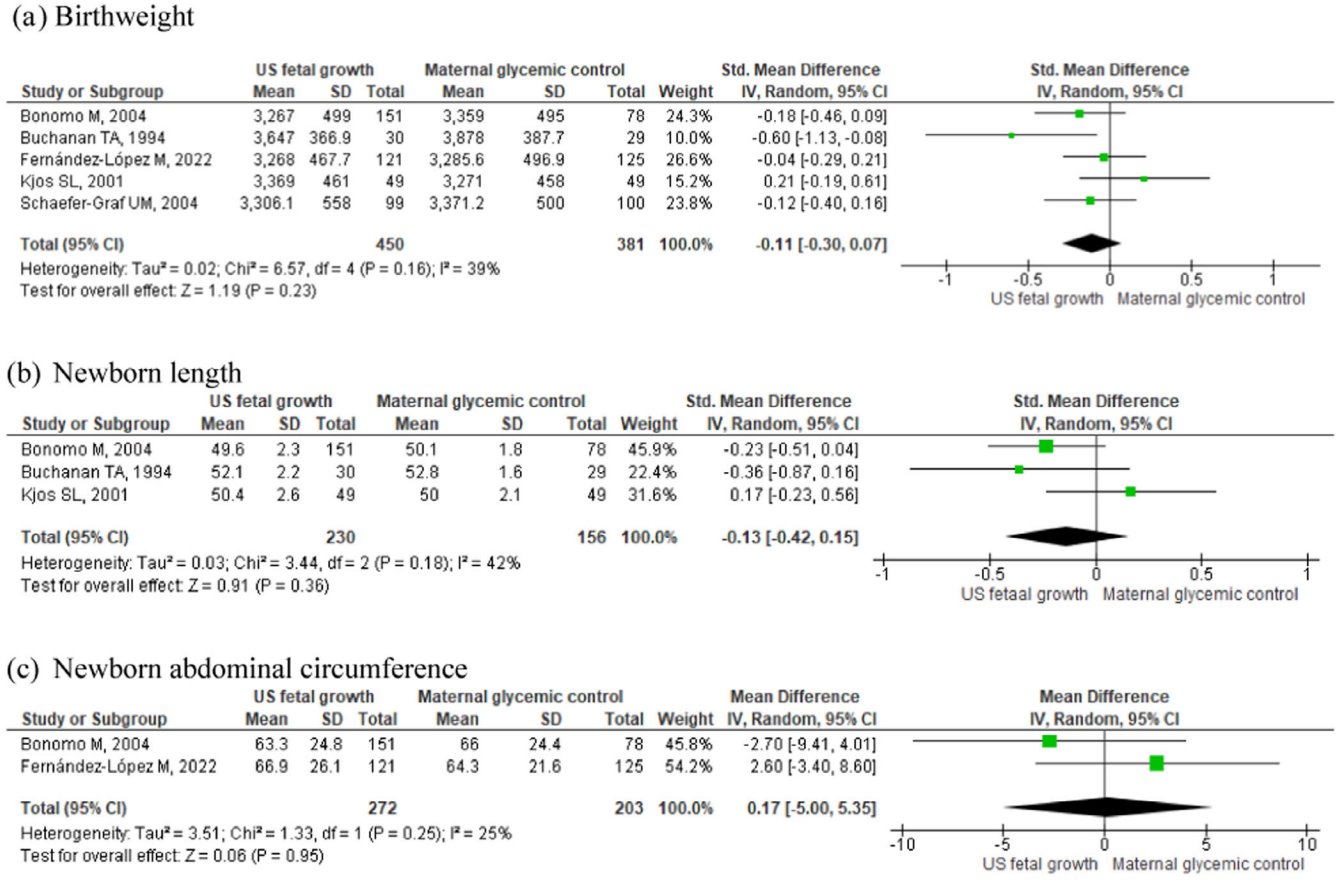
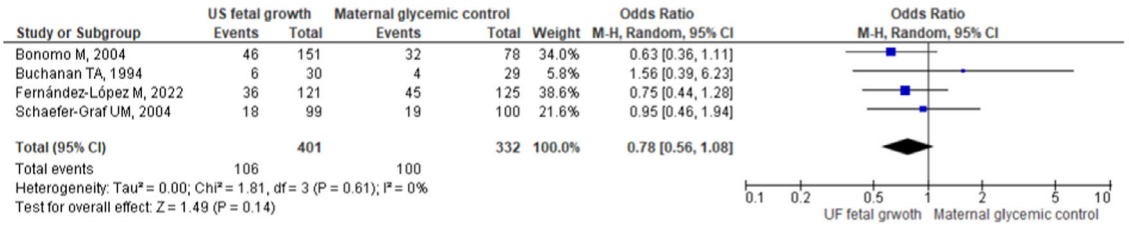


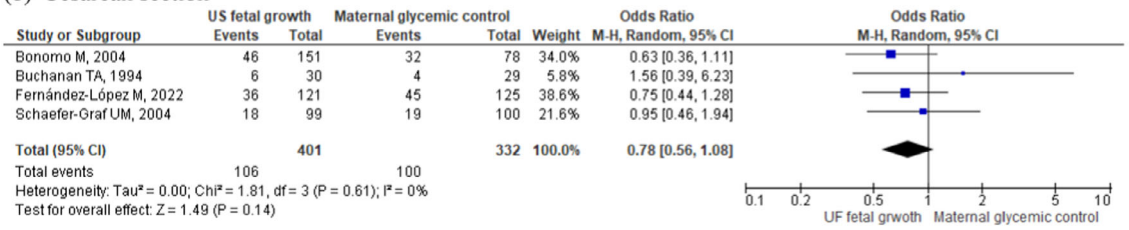
FIGURE 3 Forest plots of studies comparing (a) birthweight, (b) newborn length, and (c) newborn abdominal circumference from pregnant women with gestational diabetes mellitus in infants from pregnant women managed according to ultrasound fetal growth or maternal glycemic control.

cesarean section, and clinical and metabolic complications in neonates as compared to pregnancies without GDM.[33] These risks, trajectories, and complications are similar among different ethnic groups[4,33] and related to pregravid BMI, gestational weight gain, and prior macrosomia[10,34–36]

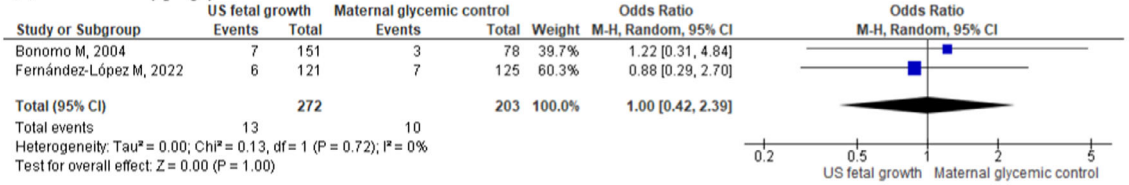
(a) Hypertensive disorders of pregnancy



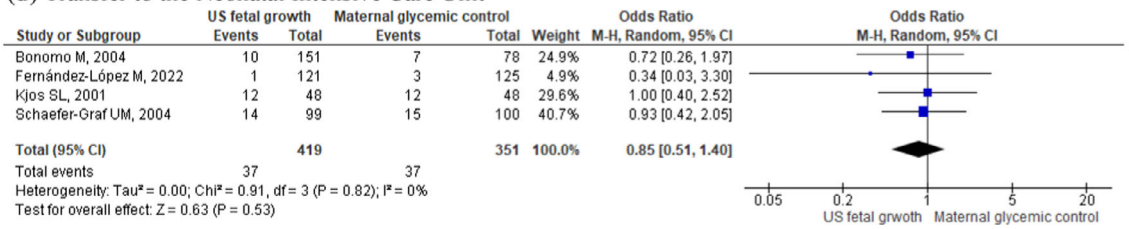
(b) Cesarean section



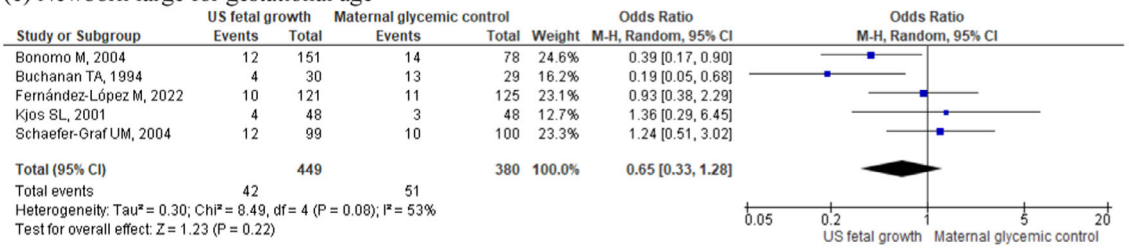
(c) Neonatal hypoglycemia



(d) Transfer to the Neonatal Intensive Care Unit



(e) Newborn large for gestational age



(f) Birthweight > 4000 grams

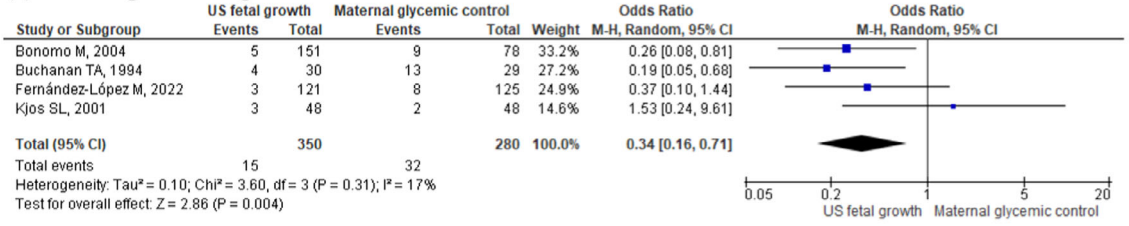


FIGURE 4 Forest plots of studies reporting odds ratios and their 95% confidence interval of rates in gestations managed according to ultrasound fetal growth or strict maternal glycemic control: (a) hypertensive disorders of pregnancy; (b) cesarean section; (c) neonatal hypoglycemia; (d) newborn transfer to the neonatal intensive care; (e) newborn large for gestational age; (f) birthweight >4000 g.

TABLE 3 Sensitivity analyses (by excluding one trial at one time) reporting standardized mean difference (SMD) and 95% confidence interval of birthweight and 95% confidence interval, *Z* score (*p* values), and heterogeneity (I^2).

Deleted study	Ultrasound fetal growth (*n*)/maternal glycemic control (*n*)	SMD (confidence interval)	*Z* score (*p*)	I^2 (%)
None deleted	459/383	−0.11 (−0.30, 0.07)	1.20 (0.16)	39
Bonomo et al.[20]	299/303	−0.10 (−0.34, 0.15)	0.77 (0.44)	51
Buchanan et al.[21]	429/354	−0.07 (−0.21, 0.07)	0.94 (0.35)	0
Fernández-López et al.[22]	338/258	−0.04 (−0.29, 0.21)	1.13 (0.26)	51
Kjos et al.[23]	410/334	−0.16 (−0.33, 0.01)	1.84 (0.07)	21
Schaefer-Graf et al.[24]	360/283	−0.12 (−037, 0.13)	0.91 (0.36)	54

Different fetal growth markers have been suggested in the diagnosis of maternal GDM. However, since it is a heterogeneous condition different pathogenetic factors may be involved, including genetic, endocrine, lifestyle, and placental hormones which adjust the pregnant women's pathophysiology to allow fetal development. However, the common nexus is insulin resistance and hyperglycemia which favors maternal metabolic dysregulation, oxidative stress, inflammation, and insulin receptor dysfunction.[33,37] Maternal weight and BMI gain may increase the risk of large gestational age fetuses in both pregnancies with and without GDM.[38] The maternal hyperglycemia that develops during GDM merits its early diagnosis and treatment during pregnancy, being the treatment reducing fetal and maternal morbidity. There are different approaches for GDM diagnosis to obtain the best obstetric outcomes.[39] Maternal glucose and glycosylated hemoglobin can be considered the first screening approach for GDM according to two recent meta-analyses,[40–42] although there is a 10% false positive rate. The current meta-analysis showed that there was no difference in glycosylated hemoglobin levels in women with GDM according to the two management protocols. Previous evidence demonstrated that maternal weight gain and high BMI may contribute to altering maternal glucose and glycosylated hemoglobin levels.[38] In our meta-analysis, there were no significant differences in both factors according to management approaches.

GDM carries a risk of complications for overgrowth neonates, large for gestational age or macrosomia (e.g., shoulder dystocia, postpartum hemorrhage, cesarean sections).[43] Pregnancy ultrasound assessment allows fetal morphologic and functional evolution, weight estimation or macrosomia, and to plan birth if needed in GDM cases.[44,45] The evidence from the current meta-analysis did not show a difference in maternal and fetal clinical and laboratory-measured outcomes, although the macrosomia rate was lower in the FMIUFG pregnancies compared to SMGA adjustments. Therefore, clinical management of GDM cases should provide adequate ultrasound assessment to identify the risk of macrosomia. In the present meta-analysis, the majority of outcomes did not display significant differences between the two studied approaches, suggesting the maternal control of GDM reached a similar level. However, the prevalence of macrosomia was significantly lower in GDM patients managed according to ultrasound assessment.

Ultrasound fetal biometry, pregnancy functional assessment, and pregnancy progression in GDM patients are representative of the endocrine and metabolic adjustments along the entire reproductive process.[46] Fetal macrosomia increases maternal and neonatal complications, including, shoulder dystocia, brachial plexus injury, birth fractures, emergency cesarean, postpartum hemorrhage, and anal sphincter injury.[47] Fetal macrosomia is an obstetric outcome related to high pre-pregnancy BMI, gestational weight gain, and GDM.[48] Our current results demonstrate that clinical management of GDM patients according to ultrasound fetal evolution benefits from therapy adjustments reducing the risk of macrosomia.

The Balsells et al[11] meta-analysis of two studies compared the management guided by the fetal growth ultrasound assessment and insulin treatment to glycemic metabolic control, showing that the first approach was associated with a lower rate of large for gestational aged and a higher rate of insulin treatment. In the present meta-analysis, we demonstrated no significant differences in gestational age at delivery, hypertensive disorders of pregnancy, cesarean section rate, birth weight, newborn length, and newborn circumference comparing the FMIUFG and the SMGA approaches. In addition, the macrosomia risk was significantly lower in FMIUFG. In addition, we demonstrated a significantly lower risk of macrosomia in GDM patients managed with the FMIUFG than with the SMGA management options. This meta-analysis confirms that fetal ultrasonography can predict fetal growth and macrosomia risk for gestational age at birth.[3] The GDM management of patients with evidence of excessive intrauterine fetal weight gain can benefit from specific treatments.[49] On the other hand, glycosylated hemoglobin is considered a suitable biomarker for GDM prediction.[50] In the present meta-analysis, there were no significant differences in glycosylated hemoglobin and glucose levels between GDM studied populations, suggesting that both clinical management options had similar efficacy in maintaining adequate glucose levels. Other factors involved in excessive fetal growth were not identified in available studies.

Limitations and strength

The present systematic review and meta-analysis have some limitations due to the intrinsic characteristics of the specific available evidence. Although all studies adhered to established GDM definitions, there was variability in study designs and sample sizes that may limit the generalizability of our findings. The meta-analyzed studies did not separate results by the newborn gender to compare reported outcomes. The few available studies do not allow adequate adjustment for confounders and do not separate results by newborn gender to compare results at diagnosis of gestational diabetes.[51,52] In addition, studies do not evaluate nutrition adjustments and exercise or other parameters such as HOMA-IR. Despite those limitations, our meta-analysis of randomized clinical trials has the strength to demonstrate that studied outcomes were not significantly different between the two management options. However, our results pointed out a significant advantage concerning the macrosomia risk for the FMIUFG compared to the SMGA strategy.

CONCLUSIONS

In this systematic review and meta-analysis, the FMIUFG versus the SMGA managements displayed similar quantitative outcomes in maternal and fetal continuous variables. However, the sole difference was that the management according to fetal ultrasound assessment was associated with a lower risk of macrosomia compared to strict glycemic management. The current wide availability, almost universal, of ultrasound assessments is progressively limiting the need to choose between one of the two options studied in this meta-analysis. A clinical exam before pregnancy is recommended to manage those factors that might contribute to the GDM risk of complications and to correct the risk factors associated with GDM pregnancies. Finally, the current wide availability, almost universal, of ultrasound assessments allows GDM patients to early diagnosis of excessive fetal growth and macrosomia risk for following appropriate ultrasound assessment and clinical management.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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How to cite this article: Fernández-Alonso AM, Monterrosa-Blanco A, Monterrosa-Castro Á, Pérez-López FR. Gestational diabetes mellitus management according to ultrasound fetal growth versus strict glycemic treatment in singleton pregnancies: A systematic review and meta-analysis of clinical trials. J Obstet Gynaecol Res. 2024. https://doi.org/10.1111/jog.16059