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Diabetology



Under the Aegis of
Diabetes India

Yearbook of

Diabetes 2026

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Section 7: DIABETES IN PREGNANCY

Section Editor: Indira Maisnam

1. Subtypes of Gestational Diabetes Mellitus are Differentially Associated with Newborn and Childhood Metabolic Outcomes

Ref: Osmulski ME, Yu Y, Kuang A, Josefson JL, Hivert MF, Scholtens DM, et al. Subtypes of Gestational Diabetes Mellitus Are Differentially Associated With Newborn and Childhood Metabolic Outcomes. Diabetes Care. 2025;48(3):390-9.

ABSTRACT

Objective: Based on insulin secretion and sensitivity, subtypes of gestational diabetes mellitus (GDM) have been identified. We investigated the hypothesis that the anthropometric and glycemic outcomes of newborns and children are differently correlated with GDM subtypes.

Methods and research design: In the hyperglycemia and adverse pregnancy outcome (HAPO) study and HAPO follow-up study, 7,970 and 4,160 mother-offspring dyads, respectively, had their newborn and child (ages 11–14 years) outcomes analyzed. GDM was categorized as either insulin-resistant GDM (insulin sensitivity < 25th percentile with preserved insulin secretion), insulin-deficient GDM (insulin secretion < 25th percentile with preserved insulin sensitivity), or mixed-defect GDM (both < 25th percentile). Maternal BMI, field center, and other pregnancy factors were adjusted for in regression models for newborn and child outcomes. Additionally, child models took into account the child's age, sex, and family history of diabetes.

Results: All three GDM subtypes were linked to birth weight and sum of skinfolds > 90th percentile when compared to mother with normal glucose tolerance. Cord C-peptide levels above the 90th percentile were linked to insulin resistance and mixed-defect GDM. An increased incidence of newborn hypoglycemia was linked to insulin-resistant GDM. Neonatal hypoglycemia and childhood obesity were linked to insulin-resistant GDM [odds ratio (OR) 1.53; 95% CI 1.127–2.08). Increased risk of childhood impaired glucose tolerance was seen in insulin resistant GDM (OR 2.21; 95% CI 1.5–3.25) and mixed defect GDM (OR 3.01; 95% CI 1.47–6.19).

Conclusion: Newborn and childhood outcomes are differently correlated with GDM subtypes. In order to provide targeted, preventative interventions early in life, it may be possible to identify at-risk offspring by better defining persons with GDM.

CRITICAL APPRAISAL

What was Known Prior to this Study?

It is known that GDM is associated with increased newborn birth weight, percentage of body fat, and cord C-peptide. GDM is associated with higher 30-min, 1-h, and 2-h glucose along with lower insulin sensitivity, insulin secretion, and disposition index, and a higher risk for childhood obesity and impaired glucose tolerance. GDM subtypes have been identified as insulin resistant, insulin deficient, and mixed defect. However, the differential effects of GDM subtypes on childhood metabolic outcomes are not clear.

What this Study Adds?

There are differential effects on childhood metabolic outcomes according to GDM subtypes. Offspring glucose intolerance is seen

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in insulin resistant or mixed-defect GDM. Offspring obesity at 5 years is seen in insulin resistant GDM. Increased cord C-peptide was seen in insulin resistant and mixed GDM and neonatal hypoglycemia was increased in insulin resistant GDM. Skin fold thickness was increased in all types. Thus, the effects of different subtypes on childhood metabolic outcomes are different and not homogeneous.

Major Strengths

The longitudinal nature of the study allowed a comprehensive picture of long-term outcomes on the effect of GDM subtypes on newborn and subsequent child metabolic outcomes. This allows for identification of at-risk offspring for better care.

Limitations

Some of the subtypes were of limited number to sufficiently identify childhood metabolic outcomes. Some cases of GDM did not fit into a single subtype.

Clinical Implications

The current study helps to offspring with metabolic risk. This will help to provide better prevention strategy.

Scope for Future Research

The influence of genetic factors, intrauterine environment including maternal metabolomics need to be studied to explain the association between subtypes and differential childhood metabolic outcomes.

2. Gestational Diabetes Mellitus Recurrence Rate and Risk Factors: A Systematic Review and Meta-analysis

Ref: Pan Y, Gu R, Wang J, Li Q, Zhang Y, Xu Y, et al. Gestational diabetes mellitus recurrence rate and risk factors: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2025;230:112949.

ABSTRACT

There are substantial short-term and long-term metabolic hazards associated with gestational diabetes mellitus (GDM). Concerns regarding GDM recurrence have increased due to changing fertility patterns, but the evidence is highly heterogeneous, which makes it difficult to identify modifiable predictors and limits evidence-based counseling. In order to address this, we searched nine electronic databases for a systematic review and meta-analysis. We found 30 trials with 30,524 women, 13,610 of whom had recurrences. There was significant heterogeneity (I^2 = 97.7%; $p < 0.001$, range: 30.87–73.75%), primarily caused by variations in diagnostic criteria, the pooled recurrence rate was 50.7% [95% confidence interval (CI) 46.6–55.2]. Ten important risk factors were found in the metabolic, obesity-related, and maternal domains. The best predictors were advanced mother age [subsequent pregnancy ≥ 35 years: odds ratio (OR) = 3.408; 95% CI 2.591–4.482] and prepregnancy obesity (BMI ≥ 30 kg/m^2 BMI ≥ 25 kg/m^2 in index pregnancy: OR = 3.248; 95% CI 1.838–5.742; in subsequent pregnancy: OR = 2.273; 95% CI 1.463–3.530). The risk was considerably elevated by prior macrosomia (OR = 2.064; 95% CI 1.820–2.341), index-pregnancy insulin therapy (OR = 2.353; 95% CI 1.351–4.098), early subsequent-pregnancy hyperglycemia (OR = 2.665; 95% CI 2.022–3.513), and hypertriglyceridemia (OR = 2.022; 95% CI 1.548–2.641). Initial diagnostic criteria and patient-specific characteristics must be integrated in risk-stratified prevention.

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CRITICAL APPRAISAL

What was Known Prior to this Study?

There is recurrence in GDM. However, the rate of recurrence and the risk factors for recurrence have not been exactly identified.

What this Study Adds?

The study found that the risk of recurrence was very high though heterogeneous. The study specifically identified 10 risk factors which were robust predictors of recurrence. This study therefore adds to our knowledge about the specific factors which increase the risk of GDM recurrence which include age, BMI, elevated 1-h and 2-h glucose levels, and insulin therapy among others. This information will help in preventive and counseling measures regarding recurrence. However, though the study did not find family history of DM, weight gain during pregnancy, interpregnancy weight gain, gestational hypertension, etc., as risk factors for recurrence, these factors cannot be entirely ruled out and further studies are needed.

Major Strengths

There were stringent inclusion/exclusion criteria coupled with multivariable adjustment, with effect sizes obtained after controlling for potential confounders in the original studies. The risk of confounding bias was low.

Limitations

Racial and geographical generalizability is not possible. The difference in the diagnostic criteria was a challenge, which affected the rates of recurrence. Protective factors against recurrence were not adequately analyzed though duration and exclusivity of breast feeding were identified as protective factors.

Clinical Implications

Recurrence of GDM is high. Some robust risk factors have been identified. Focus is on counselling and prevention in those at risk.

Scope for Future Research

Diagnostic criteria need to be uniform. However, it is not clear whether uniform criteria would apply across all racial groups. More research on this is needed. Larger, heterogeneous population is needed to study the risk factors. Protected factors need to be identified. Factors which were found not to be associated with risk but are conceptually supposed to increase the risk need to be studied in more greater detail.

3. Real-time Continuous Glucose Monitoring in Pregnancies with Gestational Diabetes Mellitus: A Randomized Controlled Trial

Ref: Valent AM, Rickert M, Pagan CH, Ward L, Dunn E, Rincon M. Real-Time Continuous Glucose Monitoring in Pregnancies With Gestational Diabetes Mellitus: A Randomized Controlled Trial. Diabetes Care. 2025;48(9):1581-8.

ABSTRACT

Objective: To determine whether real-time continuous glucose monitoring (CGM; intervention) or capillary blood glucose monitoring (CBG; control) alone is more effective in increasing the percent glucose time in range (%TIR) in pregnant patients with gestational diabetes mellitus (GDM).

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Methods and research design: Pregnant women with GDM who were at least 20 weeks pregnant participated in an open-label, single-center, randomized controlled trial. The use of real-time CGM plus adjunctive CBG versus CBG alone for glucose monitoring was randomly assigned (2:1) to the subjects. The intervention group received training on how to use the Dexcom G6 CGM system continuously from enrollment until delivery admission. During the course of the trial, the control group received blinded CGM roughly every 20 days and employed CBG monitoring four times a day. The CGM %TIR, which was defined as 60–140 mg/dL (3.3–7.8 mmol/L) from trial enrollment until hospital admission during delivery, was the main outcome.

Results: Between February 2021 and June 2023, 111 participants were enrolled (n = 74 in the intervention group and n = 37 in the control group). There were no statistically significant variations in the groups' demographics. At 60–140 mg/dL, the CGM group's %TIR ±SD was considerably higher (93 ± 6 minutes vs. 88 ± 14 minutes; p = 0.027). Key secondary CGM measure outcomes showed that, in comparison to the control group, the intervention group had significantly higher daytime TIR with lower 24-hour and daytime mean glucose and percent time > 140 mg/dL.

Conclusion: Among GDM patients, we showed a significantly greater %TIR using real-time CGM as opposed to CBG glucose monitoring. To find out if lowering CGM glucose levels can enhance prenatal and neonatal outcomes, more research is required.

CRITICAL APPRAISAL

What was Known Prior to this Study?

The Continuous Glucose Monitoring in Women With Type 1 Diabetes in Pregnancy Trial (CONCEPTT) in pregnant type 1 diabetes (T1D) showed that RT-CGM improved glycemic and neonatal outcomes. However, the evidence of benefit with RT-CGM use in GDM is scarce.

What this Study Adds?

CGM metrics like TIR, mean blood glucose concentration, better daytime TIR and lower daytime and 24-h TAR was better with the use of RT-CGM and CBG compared to CBG use alone. However, as there was no difference in the rate of perinatal, delivery and neonatal outcomes, it needs to be determined in larger studies if this better glycemic metrics translate into better outcomes.

Major Strengths

One of the few studies comparing combined RT-CGM and CBG; with CBG monitoring. The CBG and CGM data were well-characterized in the study.

Limitations

This was a single center study. The study was not powered to assess pregnancy and neonatal outcomes.

Clinical Implications

It needs to be seen if the large amount of data that is provided by CGM is actually required to favorably affect pregnancy outcomes in GDM; or whether such excess data is redundant. Based on current evidences, it appears the use of CBG monitoring is sufficient in GDM.

Scope for Future Research

It needs to be seen if the better CGM metrics with use of RT-CGM along with CBG; compared to only CBG monitoring actually translates to favorable pregnancy outcome.

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4. Lack of Validity of the Glucose Management Indicator in Type 1 Diabetes in Pregnancy

Ref: Meek CL, Feig DS, Scott EM, Corcoy R, Murphy HR; CONCEPTT Collaborative Group. Lack of Validity of the Glucose Management Indicator in Type 1 Diabetes in Pregnancy. Diabetes Care. 2025;48:1323-8.

ABSTRACT

Objective: Although the glucose management indicator (GMI) is frequently employed in place of HbA1c, very little is known about its use during pregnancy. We evaluated GMI accuracy and correlations with pregnancy outcomes in individuals with type 1 diabetes.

Methods and research design: We used logistic/linear regression and Bland–Altman plots to examine HbA1c, continuous glucose monitoring (CGM) measures, GMI at 12, 24, and 34 weeks' gestation, and outcomes in 220 women from the Continuous Glucose Monitoring in Women With Type 1 Diabetes in Pregnancy Trial (CONCEPTT).

Results: During pregnancy, GMI equations were less accurate and more biased, especially during the first and third trimesters. The ability of GMI and mean CGM glucose to predict pregnancy outcomes was comparable. Over time in range (63–140 mg/dL; 3.5–7.8 mmol/L), time above range (> 140 mg/dL; > 7.8 mmol/L), and average CGM glucose concentrations, GMI did not provide any additional predictive potential.

Conclusion: In pregnant women with type 1 diabetes, GMI is not a reliable substitute for HbA1c.

CRITICAL APPRAISAL

What was Known Prior to this Study?

Glucose management indicator (GMI) has been used as an approximation of HbA1c in nonpregnant individuals. Earlier study of GMI in type 1 diabetes (T1D) pregnancy had shown that, it is not suitable to be a replacement with HbA1c; but its association with outcomes was not studied.

What this Study Adds?

GMI performed less accurately as an approximation of HbA1c in pregnancy; associations and bias varied according to trimester. GMI did not predict additional outcomes over average glucose. Pregnancy outcomes at 34 weeks were better predicted with HbA1c than GMI. HbA1c or alternative CGM metrics, such as time in range or time above range, offer similar or better predictive capability for pregnancy outcomes compared to GMI.

Major Strengths

Study population was well characterized and was longitudinally followed up during pregnancy.

Limitations

GMI was calculated based on shorter (6 days) CGM data. Whether longer CGM data would provide additional information is not known. There was less ethnic diversity.

Clinical Implications

CGM metrics and HbA1c are the best currently available options for monitoring and outcome prediction in GDM.

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Scope for Future Research

There is a need to identify the pregnancy-related factors that determine GMI in pregnancy before it can be used safely in pregnancy to assess glycemic control and pregnancy outcomes.

5. Metformin Safety during Pregnancy in Women with Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis of Maternal, Neonatal, and Long-term Outcomes

Ref: Brinkmann MLS, Krasilnikoff NJ, Chaaban MA, Luef BM, Newman C, Dunne F, et al. Metformin safety during pregnancy in women with gestational diabetes mellitus: A systematic review and meta-analysis of maternal, neonatal and long-term outcomes. Diabet Med. 2025:e70173.

ABSTRACT

Aim: This systematic review and meta-analysis assessed the safety and efficacy of metformin in managing gestational diabetes mellitus (GDM), focusing on maternal, neonatal, and long-term outcomes. While lifestyle changes are first-line treatment, pharmacological therapy is often required. Insulin, the standard treatment, has drawbacks including weight gain, neonatal hypoglycemia, and maternal anxiety. Metformin is a promising alternative due to its insulin-sensitizing effects, but concerns remain about placental transfer and long-term effects on offspring.

Methods: A systematic search was conducted in PubMed and Embase up to 29 August 2024, including randomized controlled trials (RCTs) and follow-up studies. Primary outcomes were neonatal hypoglycemia, birthweight, and long-term metabolic outcomes. Study quality was assessed using risk of bias (RoB) 2.0 and ROBINS-I. Data were synthesized using the inverse variance heterogeneity (IVhet) model.

Results: Ten RCTs were included. Metformin was associated with a statistically significant reduction in neonatal hypoglycemia [odds ratio (OR) 0.65; 95% CI 0.46–0.92] and lower birthweight [MD −68.96 g; 95% confidence interval (CI) −108.34 to −29.57]. A nonsignificant trend toward reduced LGA risk was observed. No significant differences in prediabetes, diabetes, or insulin resistance were found. Long-term outcomes in children remain uncertain due to limited and heterogeneous follow-up data.

Conclusion: Metformin appears safe and effective in GDM management, but more data are needed on long-term outcomes.

CRITICAL APPRAISAL

What was Known Prior to this Study?

Balsells et al., in a systematic review and meta-analysis, provided evidence supporting metformin as a viable alternative to insulin in pregnancy. Farrar et al., in a systematic review and meta-analysis incorporated newer trials and reaffirmed metformin's benefits across a spectrum of pregnancy outcomes. Although no teratogenic effects have been reported, concerns regarding use of metformin during

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pregnancy persist. Metformin crosses the placenta, resulting in comparable maternal and fetal concentrations. Studies also indicated that metformin may influence fetal metabolic programming, with potential long-term consequences for offspring. In utero exposure to metformin has also been linked to a greater prevalence of obesity and increased waist to height ratios in children.

What this Study Adds?

Metformin use in pregnancy showed statistically significant reduction in neonatal hypoglycemia and a modest reduction in birthweight.

Metformin appears to be safe and effective in gestational diabetes.

Major Strength

This systematic review focused exclusively on GDM and did not combine with type 2 diabetes in pregnancy, which enhances clinical specificity.

Independent screening was performed by two blinded reviewers, with third reviewer resolved any disagreements or uncertainties. Involvement of multiple-blinded reviewers in data extraction helped to reduce potential bias and improve the consistency of results.

Use of Inverse variance heterogeneity model (IVhet model) offers more robust confidence intervals than the traditional random effects model and reduces the risk of underestimating uncertainty, in presence of low or moderate heterogeneity.

In this systematic review, effect estimates were expressed as OR rather than risk ratios (RRs). Logittorisk module was used to convert ORs into absolute risk differences and numbers needed to treat or harm (NNT/NNH) across assumed baseline risks.

Limitations

Long-term outcomes for mothers and offspring remain uncertain due to limited and heterogeneous follow-up data.

A threshold of > 100 patients in RCTs were kept as inclusion criteria in this systematic review. As a result, potentially meaningful effects observed in smaller trials were not captured.

The analysis was further complicated by variability in study populations, treatment protocols, definitions of outcomes, variations in glycemic targets, dosage regimens, and maternal baseline characteristics across the included trials.

Clinical Implications

This systematic review supports metformin as a viable treatment option for managing GDM, specially in patients who refuse to take insulin.

But clinical management should remain individualized, considering patient preferences, clinical context, and resource availability.

Scope for Future Research

Future studies should focus on standardizing outcome definitions, especially birthweight, gestational weight gain.

Adoption of the recently developed core outcome set (COS) for reporting of studies on prevention and treatment of GDM, which includes 14 key short-term maternal and neonatal outcomes, can improve consistency.

Large-scale, multicenter trials with diverse populations to improve generalizability are needed.

Longitudinal studies are needed to assess the long-term health of mothers and their offspring, including metabolic, developmental, and cardiovascular outcomes.

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