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Review Article

Pregnancy Outcomes in Indian Women with Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis

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Abstract

Background: Gestational diabetes mellitus (GDM) is a significant pregnancy complication linked to adverse maternal and fetal outcomes. The rising prevalence of GDM is emerging as a public health challenge. We aimed to explore the association between GDM and adverse pregnancy outcomes in India.

Methods: A systematic search was performed to identify eligible studies on gestational diabetes mellitus (GDM) and adverse pregnancy outcomes in India based on inclusion & exclusion criteria. The data was analyzed using R Studio. This systematic review and meta-analysis followed PRISMA guidelines and was registered with PROSPERO.

Results: Women with GDM had higher odds of exposure to adverse maternal outcomes such as cesarean section, postpartum hemorrhage, gestational hypertension, and large-for-gestational-age births. Similarly, GDM significantly increased the odds of adverse fetal and neonatal outcomes, including preterm birth, macrosomia, stillbirth, hypoglycemia, hyperbilirubinemia, congenital malformations, and shoulder dystocia. These findings highlight the increased risk burden posed by GDM on both maternal and fetal health outcomes.

Conclusion: GDM poses a substantial risk to both maternal and fetal health, contributing to multiple complications. Early detection and effective management strategies are crucial to mitigating adverse pregnancy outcomes in affected women.

Keywords: Gestational diabetes mellitus; Maternal health; Pregnancy outcomes; Fetal outcome; Meta-analysis; India

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that is first identified during pregnancy, regardless of diet or insulin treatment (1).

GDM is common during pregnancy, and is associated with unfavorable maternal and fetal health outcomes (2). It is caused by the reduced function of β-cells in the pancreas, leading to insulin resistance. The various risk factors associated

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with GDM reported were found to be high BMI, history of diabetes in the family, infertility, and obstetric history (abortions, pre-eclampsia, diabetes in a previous pregnancy, macrosomia, prematurity).

According to the International Diabetes Federation, gestational diabetes affects 14% of women globally (3). The prevalence varies from 3.4% to 22% across various nations (3-5), whereas in India, the prevalence ranges from 1% (aged between 15 to 19 years) to 14.8% (aged above 30 years) (1,2,6).

Over the years, the cases of GDM have risen in urban areas as compared to rural areas, which represents a potential public health concern. In 2021, the urban population bore a disproportionate burden of diabetes, with 360 million cases compared to 176.6 million in rural areas (7). Risk factors, such as high maternal age, current lifestyle practices, physical inactivity, and the increasing burden of obesity, put women in the loop of GDM, and their children have a high chance of developing type 2 diabetes in the future.

The prognosis of the disease imposes a huge financial burden on the healthcare system and brings a lot of challenges. However, prevention is the key to addressing the burden of GDM in women. Various studies found a positive link between GDM and adverse fetal outcomes, although the results were not definitive (8,9,10). It is recommended to conduct routine screenings for GDM between the 24th and 28th weeks of pregnancy for expectant women. Studies highlight the critical importance of maintaining optimal blood sugar control in the management of GDM (11,12).

Numerous studies have highlighted the link between GDM and pregnancy outcomes; a systematic synthesis of these findings is necessary to offer robust evidence for policymakers and practitioners in the Indian context (9,10,13,14). This review aimed to highlight the evidence on the relationship between GDM and adverse fetal and maternal outcomes in India.

Methods

This meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a standardized framework for reporting systematic reviews and meta-analyses (15). To enhance transparency and reduce bias, the study was registered with PROSPERO (Registration No. CRD42024570037).

The review's Population Exposure Comparator and Outcomes (PECO) question has been defined, specifying the population (patients with GDM), exposure (GDM), comparator (no comparator), and outcomes (adverse pregnancy outcomes that included the maternal outcomes such as cesarean section, postpartum hemorrhage, gestational hypertension, premature rupture of membranes, and large for gestational age and the fetal and neonatal outcomes such as preterm birth, stillbirth, fetal death, hyperbilirubinemia, hypoglycemia, congenital malformations, macrosomia, and shoulder dystocia.). No participants were included in this study; therefore, approval from the institutional ethics committee and written informed consent were not required.

Information sources

We performed a comprehensive search from inception until 22nd July 2024. The search strategy utilized MeSH/all term descriptors and encompassed terms such as: "gestational diabetes mellitus" OR "gestational diabetes" OR "maternal diabetes mellitus" AND "pregnancy outcome" OR "obstetric complication" OR "pregnancy disorder" OR "fetal health" OR "fetus outcome" OR "cesarean section" OR "premature rupture of membranes" OR "premature labor" OR "eclampsia and preeclampsia" AND "Indian" OR "India" OR "Asia" OR "southeast Asia". Adjustments were made to account for variations in controlled vocabulary and syntax rules (Supplemental file Table 1). Additionally, the reference lists of relevant studies were manually screened to identify additional eligible studies. However, the

authors did not contact experts in the field to seek further published or unpublished studies.

Inclusion Criteria

The inclusion criteria were defined based on the PECO framework, incorporating observational and cohort studies published in English that included patients aged 18 years and older with GDM. Eligible studies were required to report maternal and/or fetal outcomes as per the PECO framework. Exclusion criteria included studies with fewer than 30 participants, duplicate cohorts, and those lacking sufficient individual-level data on patients with GDM. Additionally, case-control studies, case reports, editorials, commentaries, clinical practice guidelines, expert opinions, and review articles were excluded.

Study Selection and Data Extraction

Articles were selected according to predefined inclusion and exclusion criteria (Table 1). Two independent reviewers screened the titles and abstracts based on these criteria, and full texts were retrieved for studies that met the inclusion requirements. Eligibility was independently assessed by both reviewers, and in cases requiring clarification, authors were contacted via email. Data extraction and synthesis were performed for all eligible studies, with reasons for exclusion carefully documented. Any discrepancies regarding study selection were resolved through discussion. Key study details, including study ID, design, population characteristics, and main outcomes, were systematically recorded using an extraction form created in Microsoft Excel 2021.

Table 1: Inclusion and exclusion criteria for study selection

Inclusion criteria
Studies involving pregnant women with GDM
Observational studies
Studies published in the English language
Conducted in India
Included only peer-reviewed journal full-text articles
Exclusion criteria
Studies conducted outside India
Non-peer-reviewed articles
Other than an observational study design

Quality and Risk Bias Assessment

The methodological quality of each section of the studies (Title, Abstract, Introduction, Methods, Results, Discussion, and other information) was assessed by utilizing a Newcastle-Ottawa Scale (NOS) for observational studies (16). Two reviewers independently assessed the quality of each study. The tool comprises 9 items that evaluate elements in observational studies. When insufficient information was available to assess a specific item, we did not assign any stars, indicating a high risk of bias. Each article's quality was considered 'good' if it had a score of 7 or higher, and 'poor' if the score was below seven. For this review, only studies with an NOS score of 7 or higher were considered for inclusion. The studies selected for analysis had scores from 7 to 9. These scores reflect the overall quality and risk bias of the studies included in this review (Supplemental file; Table 2).

Data synthesis and analysis

A meta-analysis was conducted to estimate the pooled prevalence of adverse pregnancy outcomes among patients with GDM using a random-effects model with 95% confidence intervals. Only studies that reported adverse pregnancy outcomes were included in the analysis. Heterogeneity was assessed using the I^2 statistic, with the following interpretation: 0%–40% as potentially insignificant, 30%–60% as moderate, 50%–90% as substantial, and 75%–100% as considera-

ble heterogeneity. A random-effects model was applied when heterogeneity ranged from moderate to substantial. Sensitivity and subgroup analyses were performed as needed to investigate heterogeneity and the influence of study characteristics on outcomes. All statistical analyses were conducted using R Studio (version 4.2.3), with the pooled prevalence calculated via the "metaprop" command. Publication bias for the primary outcome was not assessed due to the inclusion of fewer than 10 studies.

Results

Literature selection

A total of 681 articles were identified through electronic database searches. After removing 163 duplicates, 518 articles remained. Titles and abstracts screening was done based on inclusion criteria, which led to the exclusion of 497 articles. This left 21 articles for full-text screening. Of these, 16 articles were excluded because they did not investigate the role of GDM on adverse pregnancy outcomes between experimental and control groups, were not primary studies, or were duplicates. Ultimately, 5 articles were included in the final analysis (Fig. 1).

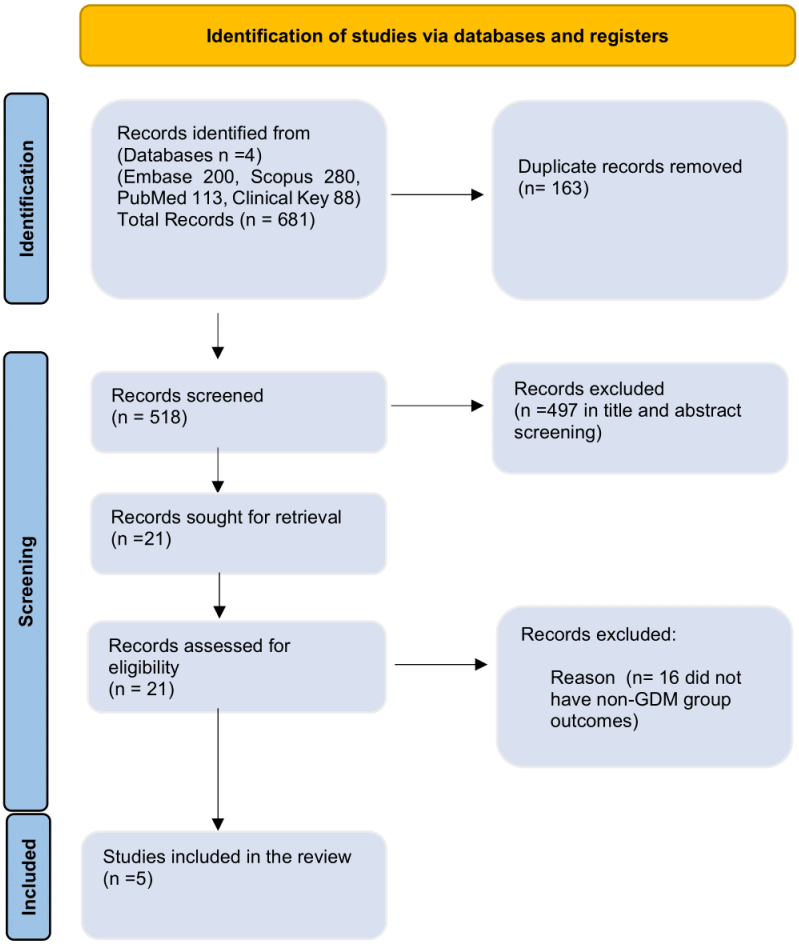

Fig. 1: PRISMA 2020 flow diagram of the study selection

The characteristics of selected studies are depicted in Table 2. Among the five studies included, two studies utilized a prospective observational study design, the other two studies were cohort studies, and the remaining one was a cross-sectional observational study design. All studies were conducted in the Indian setting. All five studies examined blood glucose by following DIPSI (Diabetes in Pregnancy Study Group India) criteria based on the WHO guidelines or by IADPSG (International Association of Diabetes and Pregnancy Study Groups) (17).

Table 2: Characteristics of selected studies

Study	Study design	Problem: GDM	Characteristics of Participants	Study population/ subjects/ participants	Outcome
Jain (11)	Prospective cohort study	Stillbirth, Neonatal death, perinatal death, congenital malformations, PIH, LBW, Jaundice, APH/PPH were associated with higher odds as compared to non GDM group (relative risk >1 in every case).	Diagnosis of GDM= 24-28 weeks	7641 pregnant women with GDM	Stillbirth, neonatal death, perinatal death, c-section, congenital malformations, LBW, PIH, PPH/ APH, Jaundice
Prakash (14)	Prospective observational study	GDM is associated with Hypertension, hypothyroidism, obesity, and lipid abnormalities	Mean age=28 yrs Diagnosis of GDM=30 weeks Mean BMI= 28.8	148 women with gestational diabetes GDM mean age 28 ±4.4 v/s control age 27.9 ± 3.8)	Preeclampsia, Prolonged labour, PROM, perineal tear, dystocia, prematurity, respiratory distress, hypoglycemia, foetal demise, congenital anomalies
Trivedi (37)	Prospective observational study	The prevalence of stillbirths, macrosomia, and neonatal intensive care unit (NICU) admissions was higher in the GDM group than in the non-GDM group.	Diagnosis of GDM= 24-28 weeks	210 patients between 24 and 28 weeks of gestation, attending the antenatal clinic	Stillbirth, macrosomia, hypoglycemia, Hyperbilirubinemia, PIH, C-section, Abruptio placenta, vaginal candidiasis, PROM, dystocia, PPH
Bahl (8)	Cohort study	Prediabetes, Women age & High BMI had a significantly higher risk of developing GDM	Mean age= 24.7±3.0 Diagnosis of GDM at or after 28 weeks Mean BMI= 23.1± 4.2	2294 women (mean age of GDM 23.5 ± 3.1 v/s No GDM 24.7 ± 3.0)	Stillbirth, preterm birth, LGA, c-section
Biju (13)	Cross-sectional observational study	The rates of cesarean delivery and PPH were also higher in the GDM group compared to the non-GDM group.	Mean age=28 yr Diagnosis of GDM= 24-28 Mean BMI= 23.37±2.7	518 pregnant women (28±5.034 years in the non GDM and 29.23±5.45 years in the GDM group)	Gestational hypertension, polyhydramnios, c-section, PPH, macrosomia, fetal hypoglycemia, fetal death

Footnote: APH, antepartum haemorrhage; BMI, body mass index; GDM, gestational diabetes mellitus; PIH, pregnancy-induced hypertension; LBW, low birth weight; PPH, postpartum haemorrhage; PROM, premature rupture of membranes; LGA: large-for-gestational-age

Maternal outcomes with GDM

The random-effects meta-analysis showed that women with gestational diabetes mellitus had a higher likelihood of experiencing adverse maternal outcomes compared to the control group, with substantial heterogeneity across studies. Sub-group analyses indicated increased risks for cesarean section, postpartum hemorrhage, gestational hypertension, premature rupture of membranes, and delivery of large-for-gestational-age infants. No significant variation in effect sizes across studies was observed, as illustrated in Fig. 2.

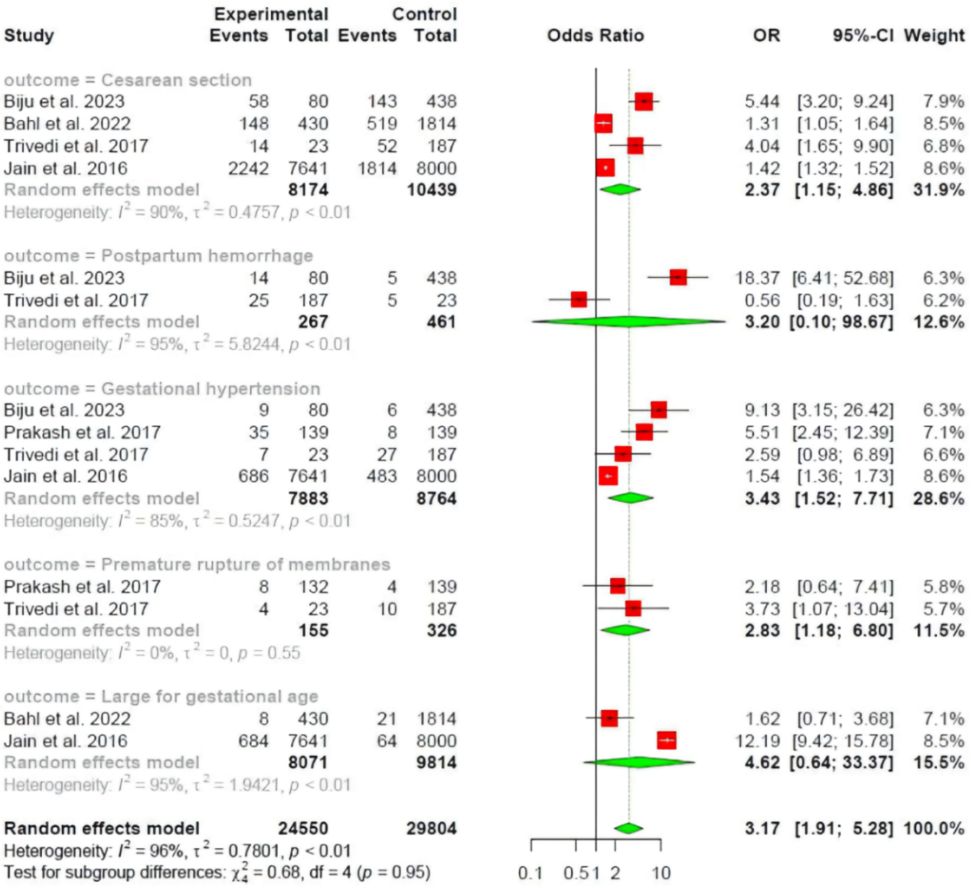

Fig. 2: A Forest plot: Pooled effect estimates of the association between GDM and maternal health outcomes

Fetal outcomes with GDM

With regard to adverse fetal outcomes, the present meta-analysis indicated that women with gestational diabetes mellitus had a higher likelihood of experiencing overall adverse fetal outcomes, with substantial heterogeneity across studies. Sub-group analyses showed particularly increased risks of macrosomia, congenital malformations, and shoulder dystocia. Elevated risks were also observed for hypoglycemia, preterm delivery, hyperbilirubinemia, and stillbirth. No significant variation in effect sizes across studies was observed, as illustrated in Fig. 3.

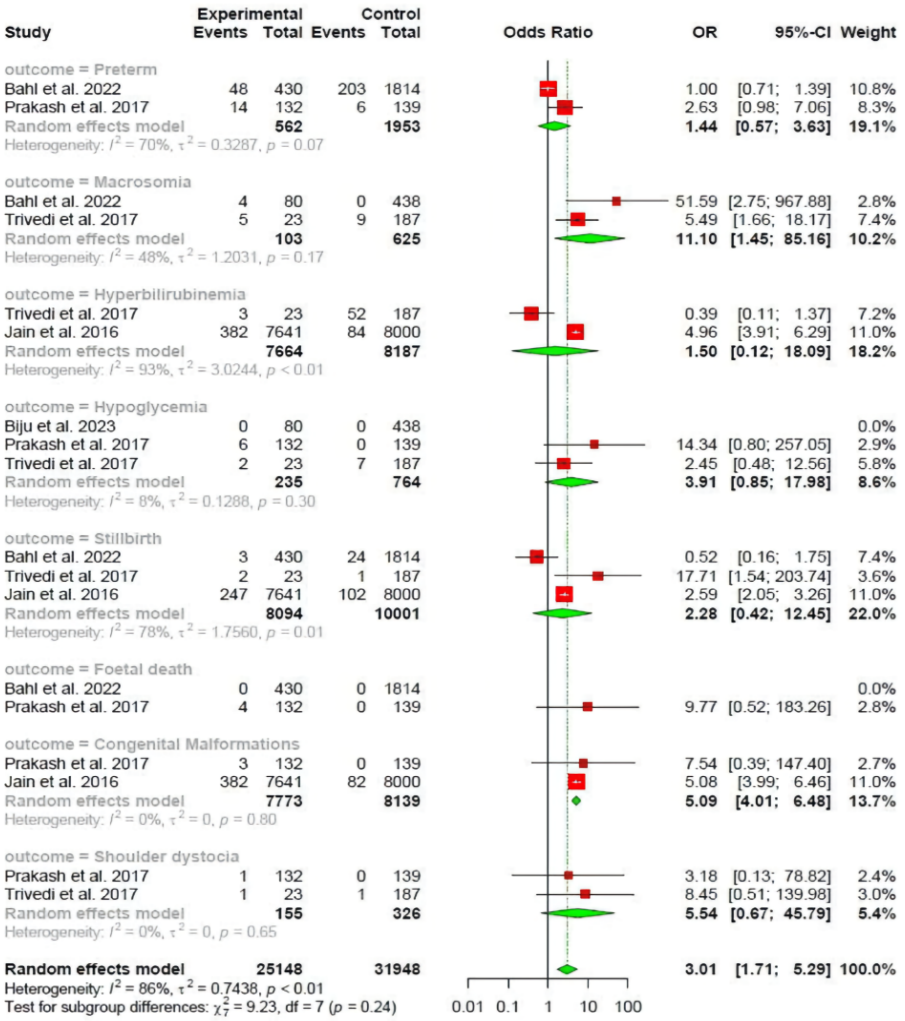

Fig. 3: A Forest plot: Pooled effect estimates of the association between GDM and fetal health outcomes

Discussions

Research indicates that the increased burden of GDM contributes to a significant public health challenge among pregnant women in India (2,18). This study offers a comprehensive analysis based on quantitative estimates of the relationship between GDM and pregnancy outcomes through a systematic search and meta-analysis. It provides updated, essential information on GDM and pregnancy outcomes. Several studies were conducted to estimate the effects of GDM and maternal outcomes such as c-sections (19), spontaneous abortion (20), gestational hypertension (21), LGA (22), preeclampsia (23,24), PPH (25), PROM (26), or polyhydramnios (26,27). Whereas the current study reports higher odds of exposure to c-section, gestational hypertension, LGA, PPH, and PROM among women with GDM. Specifically, the increased risk of LGA in the present study can be attributed to elevated maternal blood glucose levels, which cross the placenta and stimulate excessive fetal insulin production, leading to accelerated fetal growth and, consequently, larger infants (28). A study reported the incidence of emergency cesarean delivery was significantly higher among nulliparous women with GDM, who had nearly twice the risk compared with women without GDM (AOR 1.9, 95% CI 1.03–3.5, P = 0.039) (29). We reported

an overall effect of 3.17 times higher exposure to maternal outcomes among GDM women, whereas another study reported (OR: 0.8, 0.7 -0.9) (30). This difference could be attributed to differences in study populations, diagnostic criteria, and management practices for GDM. Another study reported a lower odds ratio, which reflects improved management and early intervention strategies in their study cohort, highlighting the importance of context in interpreting these outcomes (31).

Numerous studies have reported fetal outcomes, including congenital malformations (32), hypoglycemia (33), macrosomia (34), hyperbilirubinemia (35), preterm delivery (36), shoulder dystocia (37), and stillbirth (38). The findings of this study indicate a significant association between GDM and adverse fetal outcomes, highlighting the increased risks posed to fetal health in women with GDM. The meta-analysis revealed an overall odds ratio (OR) of 3.01 (95% CI: 1.71–5.29) for adverse fetal outcomes, corroborating the findings of previous research (19). The current study reports higher odds of shoulder dystocia and macrosomia due to excess maternal glucose, which triggers increased fetal insulin and rapid growth. This larger fetal size raises the risk of shoulder dystocia, where the infant's shoulder gets trapped during delivery (34). Few studies with significant findings depicted similar results, emphasizing the increased risk of several congenital anomalies in infants born to mothers with GDM (39-41). The consistency of our findings with existing literature strengthens the evidence linking GDM to adverse pregnancy outcomes.

The key strength of our study includes 1) the comprehensive selection of studies conducted exclusively in India. 2) As per the authors' knowledge, no recent meta-analysis and systematic review have been conducted that specifically examines the association between GDM and adverse pregnancy outcomes within the Indian context. 3) India is the most populous country and has the world's second-highest burden of diabetes; it is crucial to focus on maternal and child health to reduce the growing burden of non-communicable diseases (NCDs). The findings of this study provide valuable insights that can guide efforts to improve pregnancy outcomes in India, highlighting the need for targeted interventions and policies aimed at enhancing maternal and child health.

Limitation

There were limited studies conducted to examine the association between GDM and adverse pregnancy outcomes in India. The inclusion of a smaller number of studies may reduce the generalizability of findings. Most of the included studies were prospective observational designs, which observed associations between GDM and adverse pregnancy outcomes but did not establish a causal relationship.

Conclusion

The evidence from this review highlights the elevated risks associated with GDM. To achieve meaningful improvements in pregnancy outcomes, it is crucial to implement comprehensive and standardized screening programs across the country. Early detection of GDM allows for timely intervention, which can significantly reduce the likelihood of adverse outcomes. Moreover, enhancing access to quality healthcare services, particularly in rural and underserved areas, is essential to ensure that all women receive the care they need during pregnancy. Educational campaigns can help women understand the risks associated with GDM and the importance of regular monitoring and adherence to treatment plans. By fostering a greater understanding of GDM and its implications, we can empower women to take proactive steps in managing their health during pregnancy.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare no conflict of interest.

Availability of supplementary data

All supplementary data are present on the journal website. Besides, they are accessible via sending an email to the corresponding author based on a reasonable application.

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