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First-trimester fasting plasma glucose as a predictor of subsequent gestational diabetes mellitus and adverse fetomaternal outcomes: A systematic review and meta-analysis

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ABSTRACT

Background: The implication of intermediately elevated fasting plasma glucose (FPG) in the first trimester of pregnancy is uncertain.
Purpose: The primary outcome of the meta-analysis was to analyze if intermediately elevated first-trimester FPG could predict development of GDM at 24–28 weeks. The secondary outcomes were to determine if the commonly used FPG cut-offs 5.1 mmol/L (92 mg/dL), 5.6 mmol/L (100 mg/dL), and 6.1 mmol/L (110 mg/dL) correlated with adverse pregnancy events.
Data sources: Databases were searched for articles published from 2010 onwards for studies examining the relationship between first-trimester FPG and adverse fetomaternal outcomes.
Study selection: A total of sixteen studies involving 115,899 pregnancies satisfied the inclusion criteria.
Data extraction and data synthesis: Women who developed GDM had a significantly higher first-trimester FPG than those who did not [MD 0.29 mmoL/l (5 mg/dL); 95 % CI: 0.21–0.38; $P < 0.00001$]. First-trimester FPG ≥5.1 mmol/L (92 mg/dL) predicted the development of GDM at 24–28 weeks [RR 3.93 (95 % CI: 2.67–5.77); $P < 0.0000$], pre-eclampsia [RR 1.55 (95%CI:1.14–2.12); $P = 0.006$], gestational hypertension [RR1.47 (95% CI:1.20–1.79); $P = 0.0001$], large-for-gestational-age (LGA) [RR 1.32 (95%CI:1.13–1.54); $P = 0.0004$], and macrosomia [RR1.29 (95%CI:1.15–1.44); $P < 0.001$]. However, at the above threshold, the rates of preterm delivery, lower-segment cesarean section (LSCS), small-for gestational age (SGA), and neonatal hypoglycemia were not significantly higher. First-trimester FPG ≥5.6 mmol/L (100 mg/dL) correlated with occurrence of macrosomia [RR1.47 (95 % CI:1.22–1.79); $P < 0.0001$], LGA [RR 1.43 (95%CI:1.24–1.65); $P < 0.00001$], and preterm delivery [RR1.51 (95%CI:1.15–1.98); $P = 0.003$], but not SGA and LSCS.
Limitations: Only one study reported outcomes at first-trimester FPG of 6.1 mmol/L (110 mg/dL), and hence was not analyzed.
Conclusion: The risk of development of GDM at 24–28 weeks increased linearly with higher first-trimester FPG. First trimester FPG cut-offs of 5.1 mmol/L (92 mg/dL) and 5.6 mmol/L (100 mg/dL) predicted several adverse pregnancy outcomes.

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1. Introduction

The escalating rates of diabetes and obesity have coincided with the rise in the identification of both overt diabetes and gestational diabetes mellitus (GDM) during pregnancy. GDM, classically defined as an abnormal glucose tolerance first recognized during pregnancy, impacts around 14 % of pregnancies globally [1]. Hyperglycemia during pregnancy not only adversely affects maternal and neonatal health but also poses a potential risk for future cardiometabolic disorders in both the mother and the offspring.

GDM, referred to as conventional GDM (cGDM) in this article, is diagnosed during 24–28 week gestation by the traditional two-step Carpenter-Coustan criteria or the more recent one-step method proposed by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) [2]. The IADPSG, in 2010, other than modifying the diagnostic criteria of cGDM, also emphasized the importance of screening for hyperglycemia early in pregnancy, particularly for at-risk groups. Early screening aims to identify undiagnosed overt diabetes to prevent congenital malformations [3].

Most guidelines recommend using FPG, glycated hemoglobin (A1C), or oral glucose tolerance test (OGTT) for first-trimester screening [2, 4–6]. The IADPSG suggested that any one of FPG, A1C, or random plasma glucose (RPG) with subsequent confirmation, can be employed [2]. The World Health Organization (WHO) favored the use of OGTT applying IADPSG cut-offs [5], while the recent American Diabetes Association (ADA) guidelines propose FPG and A1C as the preferred tests for first trimester [4].

The recent 2023 ADA statement recommends an A1C $\geq$ 5.9 % (41 mmol/mol) or an FPG $\geq$6.1 mmol/L (110 mg/dL) as indicative of early abnormal glucose metabolism for potentially identifying pregnancies at higher risk of adverse outcomes [4]. However, it's important to note that very few studies have examined the validity of these thresholds [7]. FPG and A1C are considered simpler and easily executable options and are usually preferred over the more cumbersome OGTT in the first trimester [4,8].

The term early gestational diabetes mellitus (eGDM) has also been used for pregnancies found to have intermediately elevated glucose levels detected during screening in early pregnancy [4,9]. In eGDM, the glucose values are above the threshold used for diagnosing GDM between 24 and 28 weeks, but do not reach the cut-offs for overt diabetes. The significance of intermediately elevated glucose values is currently unclear. There is also no consensus on the criteria for diagnosis and management of eGDM.

In 2010, the IADPSG had proposed that FPG level $\geq$5.1 mmol/L (92 mg/dL) during first-trimester as diagnostic of GDM [2]. The IADPSG cut-offs were however derived from data obtained during the latter half of pregnancy, and the committee issued a clarification in 2015 advising against the use of the criteria in the first trimester [10]. However, by that time, some guidelines had already endorsed the criteria [11,12]. On the other hand, in the United Kingdom, the National Institute for Health and Care Excellence recommends using FPG $\geq$5.6 mmol/L (100 mg/dL) or 2-h plasma glucose $\geq$7.8 mmol/L (140 mg/dL) during an OGTT as criteria for diagnosing GDM, irrespective of the pregnancy trimester [13]. Diverse diagnostic criteria for eGDM contribute to the complexity in defining the condition [4,5,11,13].

Some of the studies exploring FPG cut-off points of 5.1 mmol/L (92 mg/dL) [14–16], and 5.6 mmol/L (100 mg/dL) [17], reveal an increased likelihood of adverse outcomes above these levels. Moreover, prospective studies [18–22] and retrospective analysis of medical records [23–25] associate intermediately elevated first-trimester FPG with worsened fetomaternal outcomes and the risk of cGDM. Nomograms predicting cGDM using first-trimester FPG have been developed but lack large-scale validation [26–28]. However, studies linking first-trimester FPG to adverse outcomes are mainly observational. This highlights the crucial need for well-designed clinical trials to determine the appropriate diagnostic threshold for eGDM.

This systematic review and meta-analysis explores the link between intermediately elevated first-trimester FPG and the risk of development of GDM between 24 and 28 weeks and other related fetomaternal outcomes. This is the first meta-analysis to examine the clinical implications of intermediately elevated first-trimester FPG.

2. Methods

The systematic review and meta-analysis was done using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The predefined protocol has been registered in PROSPERO with the registration number CRD42023415490.

2.1. Eligibility criteria for study selection

Utilizing the PICOS criteria, we included studies published after 2010 involving pregnant women with data available on first-trimester FPG and the occurrence of cGDM or other fetomaternal outcomes. We included studies post-2010 due to significant heterogeneity in study designs before IADPSG recommendations. Articles correlating the risk of development of cGDM to first-trimester FPG as a continuous variable were analyzed. Additionally, studies assessing FPG as a dichotomous variable at the diagnostic cut-points 5.1 mmol/L (92 mg/dL), 5.6 mmol/L (100 mg/dL), and 6.1 mmol/L (110 mg/dL) were separately examined. Case reports, case series, review articles, abstracts, and animal studies were excluded. Furthermore, studies involving interventions for eGDM in the first trimester were excluded. Two authors independently identified eligible articles based on the criteria, and any discrepancies in study inclusion were resolved through consensus.

2.2. Search strategy

We systematically searched Embase database, Web of Science, Cochrane Library, Medline (PubMed), clinicaltrials.gov, CNKI database, ctri. nic.in, and Google Scholar as either keywords or MESH terms: (fasting plasma glucose) OR (fasting glucose) OR (glucose) AND (pregnancy trimester, first). In addition, we manually searched review articles and checked reference lists of original articles to identify studies that might have been missed from the electronic search.

The primary outcome of the meta-analysis was to analyze if intermediately elevated first-trimester FPG could predict development of GDM at 24–28 weeks. Secondary outcomes included assessing whether first-trimester FPG values at cut-offs of 5.1 mmol/L (92 mg/dL), 5.6 mmol/L (100 mg/dL), and 6.1 mmol/L (110 mg/dL) could predict various pregnancy-related outcomes such as cGDM, gestational hypertension, pre-eclampsia, preterm delivery, rates of lower-segment cesarean section (LSCS), macrosomia, small for gestational age (SGA), large for gestational age (LGA), and neonatal hypoglycemia.

2.3. Data extraction and risk of bias assessment

Data extraction was conducted independently by two authors. The review encompassed the extraction of the following details from all eligible studies: author(s), publication year, title, journal, study design, participant count, age, body mass index (BMI), parity, mean or median FPG in the first trimester, criteria employed for diagnosing cGDM, as well as obstetric and neonatal outcomes. For studies that reported data as median and interquartile range, standard method (outlined by Wan) was used to convert to mean and standard deviation (SD).

Two authors assessed study bias using the Newcastle-Ottawa Scale. This scale evaluates potential bias in prospective studies based on three key aspects: participant selection, comparability, and outcomes. Participant selection includes criteria like representativeness, comparability, exposure ascertainment, and absence of the outcome at the study's outset, representativeness of the exposed cohort, comparable derivation of exposed and non-exposed participants, proper

ascertainment of exposure, and absence of the outcome of interest at the study's commencement. Comparability is based on analysis design, assigning zero points if odds ratios or relative risks relied solely on raw participant numbers. Outcome assessment considers adequacy, follow-up duration, and sufficiency. Scores on the Newcastle-Ottawa Scale range from 0 to 9, categorizing studies as low (0–3 points), moderate (4–6 points), or high (7–9 points) quality. In the event of any disagreements, consensus was achieved through discussion.

2.4. Data synthesis and analysis

We used the International System of Units (SI units) for all analyses. Continuous variables were presented as mean differences (MD), while dichotomous variables were expressed as risk ratios (RR) with 95 % confidence intervals (CI). Statistical analysis and forest plot generation were conducted using RevMan 5.4. The random-effects model was used, and the results were presented as 95 % CIs. Heterogeneity was assessed using the Chi^2 test with N-1 degrees of freedom, with a significance level of $\alpha = 0.05$, and the I^2 test. Heterogeneity was categorized as low, moderate, or high, with upper limits of 25 %, 50 %, and 75 %, respectively. N-1 degrees of freedom, with an alpha of 0.05 was used for statistical significance and for the I^2 test.

Publication bias was evaluated using Funnel Plots, as elaborated in Supplementary Fig. 1. The presence of one or more smaller studies outside the inverted funnel plot was considered indicative of significant publication bias. We graded key outcomes using the GRADE software (https://gdt.gradepro.org/app/).

3. Results

Initially, 5336 articles were identified through the search process, and after screening titles and abstracts, 217 studies were subjected to detailed evaluation (Fig. 1). Ultimately, 16 studies involving 115,899 participants met all the criteria and were included in the analysis (Supplementary Table 1 and Supplementary Table 2). The salient features of the included studies is presented in Table 1. The risk of bias for the case-control and cohort studies is outlined in Supplementary Table 3.

3.1. First-trimester FPG and development of cGDM

Eleven studies investigated the relationship between first-trimester FPG levels and the risk of developing cGDM [18–22,24–29]. Guo et al. [27] reported prospective and retrospective cohorts in the same study, which were analyzed separately. Our meta-analysis reveals that women with intermediate levels of first-trimester fasting hyperglycemia had a significantly greater risk of developing cGDM at higher FPG values [MD 0.29 mmol/L (5 mg/dL); 95 % CI: 0.21–0.38; $P < 0.00001$; $I2 = 97$ %, high heterogeneity (HH), Supplementary Fig. 1]. The included studies showed high heterogeneity that persisted even after sensitivity analysis.

3.2. Pregnancy outcomes based on first-trimester FPG ≥5.1 mmol/L (92 mg/dL)

Five studies were identified that examined the relationship between pregnancy outcomes at a first-trimester FPG ≥5.1 mmol/L (92 mg/dL)

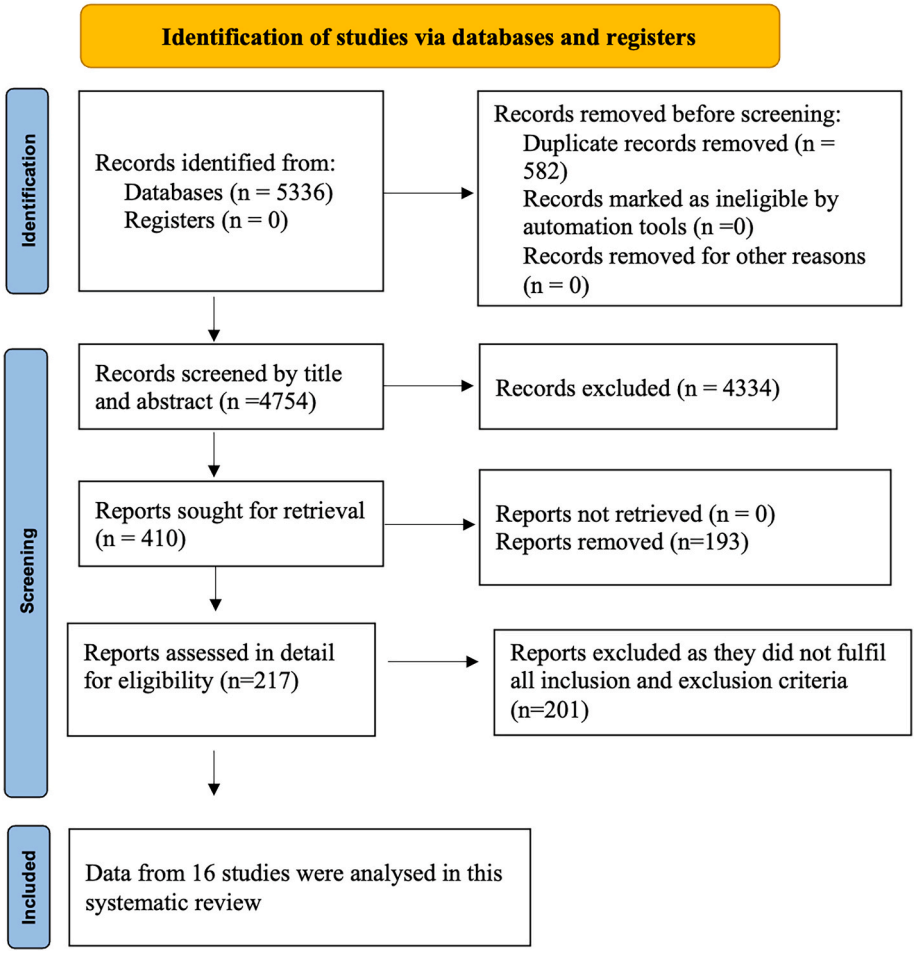

Figure-1. Flowchart elaborating on study retrieval and inclusion in this systematic review.

Table 1
Summary of findings of key outcomes of the meta-analysis.

Outcomes	Anticipated absolute effects* (95 % CI)		Relative effect (95 % CI)	N° of participants (studies)	Certainty of the evidence (GRADE)
	FPG in control group	FPG in GDM			
FPG in GDM vs controls	Mean FPG in the control group - 4.6 mmoL/l	MD 0.29 higher (0.21–0.38 higher)	–	67,466 (11 observational studies)	⨁⨁◯◯Low[a,b]

Outcomes	Anticipated absolute effects* (95 % CI)		Relative effect (95 % CI)	N° of participants (studies)	Certainty of the evidence (GRADE)
	Risk with FPG <5.1 mmol/L	Risk with FPG ≥5.1 mmoL/l			
Preeclampsia	23 per 1000	36 per 1000	RR 1.55 (1.14–2.12)	24,381 (3 observational studies)	⨁⨁◯◯Low
Gestational HTN	23 per 1000	34 per 1000	RR 1.47 (1.20–1.79)	23,623 (2 observational studies)	⨁⨁◯◯Low
Preterm Delivery	44 per 1000	57 per 1000	RR 1.30 (0.88–1.93)	46,220 (4 observational studies)	⨁◯◯◯Very low[a]
LSCS	373 per 1000	417 per 1000	RR 1.12 (0.99–1.27)	46,224 (4 observational studies)	⨁⨁◯◯Low
LGA	135 per 1000	178 per 1000	RR 1.32 (1.13–1.54)	48,433 (5 observational studies)	⨁⨁◯◯Low
Macrosomia	67 per 1000	86 per 1000	RR 1.29 (1.15–1.44)	24,842 (3 observational studies)	⨁⨁◯◯Low
SGA	42 per 1000	39 per 1000	RR 0.91 (0.77–1.07)	25,850 (3 observational studies)	⨁⨁◯◯Low
Neonatal Hypoglycemia	4 per 1000	5 per 1000	RR 1.29 (0.32–5.18)	23,223 (2 observational studies)	⨁◯◯◯Very low[c]

Outcomes	Anticipated absolute effects* (95 % CI)		Relative effect (95 % CI)	N° of participants (studies)	Certainty of the evidence (GRADE)
	Risk with FPG <5.6 mmoL/l	Risk with FPG ≥5.6 mmoL/l			
Macrosomia	67 per 1000	99 per 1000	RR 1.47 (1.22–1.79)	25,844 (3 observational studies)	⨁⨁◯◯Low
SGA	39 per 1000	33 per 1000	RR 0.84 (0.67–1.05)	24,625 (2 observational studies)	⨁⨁◯◯Low
LGA	156 per 1000	224 per 1000	RR 1.43 (1.24–1.65)	23,596 (2 observational studies)	⨁⨁◯◯Low
Preterm delivery	46 per 1000	70 per 1000	RR 1.51 (1.15–1.98)	23,599 (2 observational studies)	⨁⨁◯◯Low
LSCS	447 per 1000	475 per 1000	RR 1.12 (0.97–1.31)	23,614 (2 observational studies)	⨁⨁◯◯Low

FPG – fasting plasma glucose, GDM – gestational diabetes mellitus, HTN – hypertension, LGA – large for gestational age, LSCS – lower segment Caesarean section, SGA – small for gestational age.

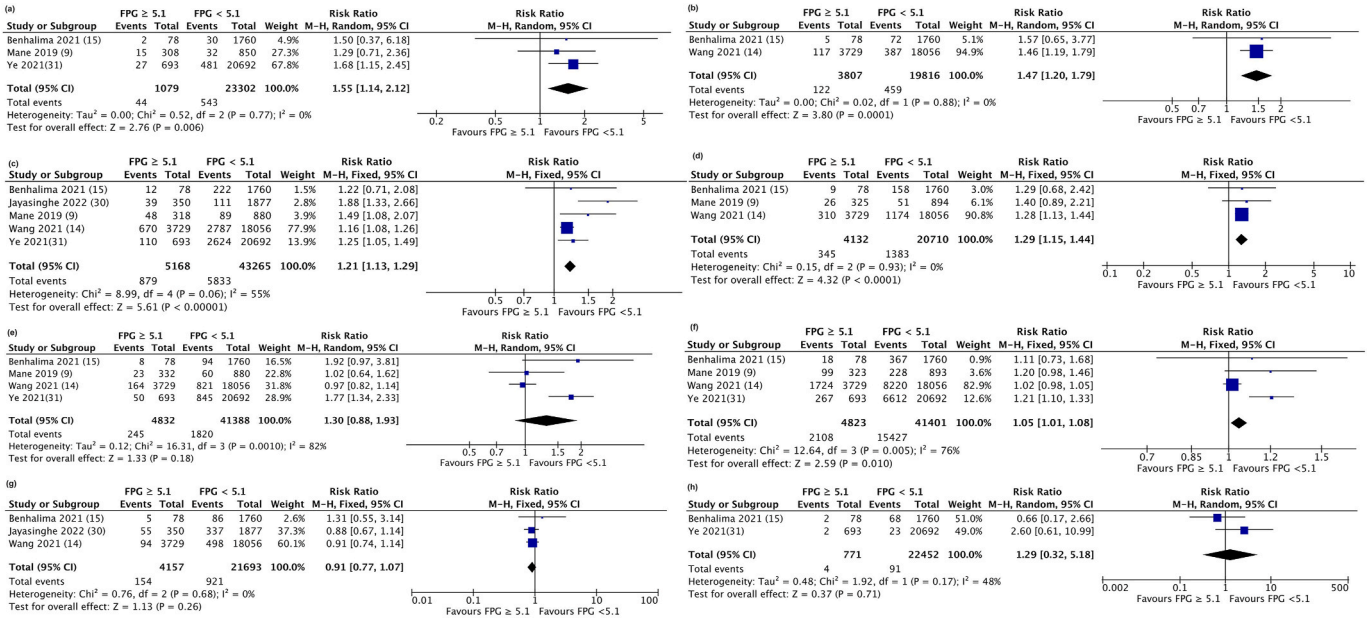

Figure-2. Forest plot highlighting the impact of fasting plasma glucose ≥5.1 mmol/L in the first trimester as compared to controls on the occurrence of (a) pre-eclampsia, (b) gestational hypertension, (c) large for gestational age, (d) macrosomia, (e) preterm delivery, (f) lower-segment Caesarean section, (g) small for gestational age, and (h) neonatal hypoglycemia. FPG – fasting plasma glucose (value in mmol/L).

[7,14,15,30,31]. Women with first-trimester FPG levels above the threshold exhibited a significantly increased risk of various pregnancy complications. A higher probability of pre-eclampsia [RR 1.55 (95% CI:1.14–2.12); P = 0.006], gestational hypertension [RR 1.47 (95% CI:1.20–1.79); P = 0.0001], LGA [RR 1.32 (95%CI:1.13–1.54); P = 0.0004], and macrosomia [RR1.29 (95%CI:1.15–1.44); P < 0.001] was seen above this cut-off (Fig. 2a–d). These findings were statistically significant and consistent across the studies included in the analysis. The risk of developing cGDM at 24–28 weeks was also significantly higher [RR 3.93 (95 % CI: 2.67–5.77); P < 0.00001; n = 2445] above this FPG threshold. However, there was no difference in the occurrence of preterm delivery, rates of LSCS, SGA, and neonatal hypoglycemia above the threshold. (Fig. 2e–h).

3.3. Pregnancy outcomes in women with first-trimester FPG ≥5.6 mmol/L (100 mg/dL)

Three studies were identified investigating the relationship between pregnancy outcomes at a first-trimester FPG ≥5.6 mmol/L (100 mg/dL) [7,14,30]. Higher FPG levels predicted the occurrence of macrosomia [RR1.47 (95 % CI:1.22–1.79); P < 0.0001], LGA [RR 1.43 (95% CI:1.24–1.65); P < 0.00001], and preterm delivery [RR1.51 (95% CI:1.15–1.98); P = 0.003]. The incidence of neonates with SGA was similar in both groups (Fig. 3a–d). The rates of LSCS were also identical [RR 1.12 (95 % CI: 0.97–1.31); P = 0.13; n = 23,614].

3.4. Other findings

The certainty of the evidence for the outcomes in this meta-analysis ranged from low to very low and is a major limitation. The funnel plots were plotted to evaluate the presence of publication bias and is depicted in Supplementary Fig. 2. Only one study assessed FPG ≥6.1 mmol/L (110 mg/dL) as a cut-off and could not be analyzed [7].

4. Discussion

The approach to intermediately elevated hyperglycemia during the first-trimester of pregnancy or eGDM is uncertain. This condition arises when plasma glucose levels in the first trimester satisfy the diagnostic criteria used for GDM between 24 and 28 weeks [8,9]. There is a lack of systematic information on fetomaternal outcomes in pregnancies with eGDM. The diagnostic cut-offs for cGDM applied during 24–28 weeks lack validation in the first trimester [2,4,5,11]. While various retrospective and prospective studies have explored the association of elevated first-trimester FPG to adverse fetomaternal outcomes, there is no consensus on the threshold at which treatment should commence. Ours is the first systematic review and meta-analysis to examine first-trimester FPG as a determinant of gestational outcomes.

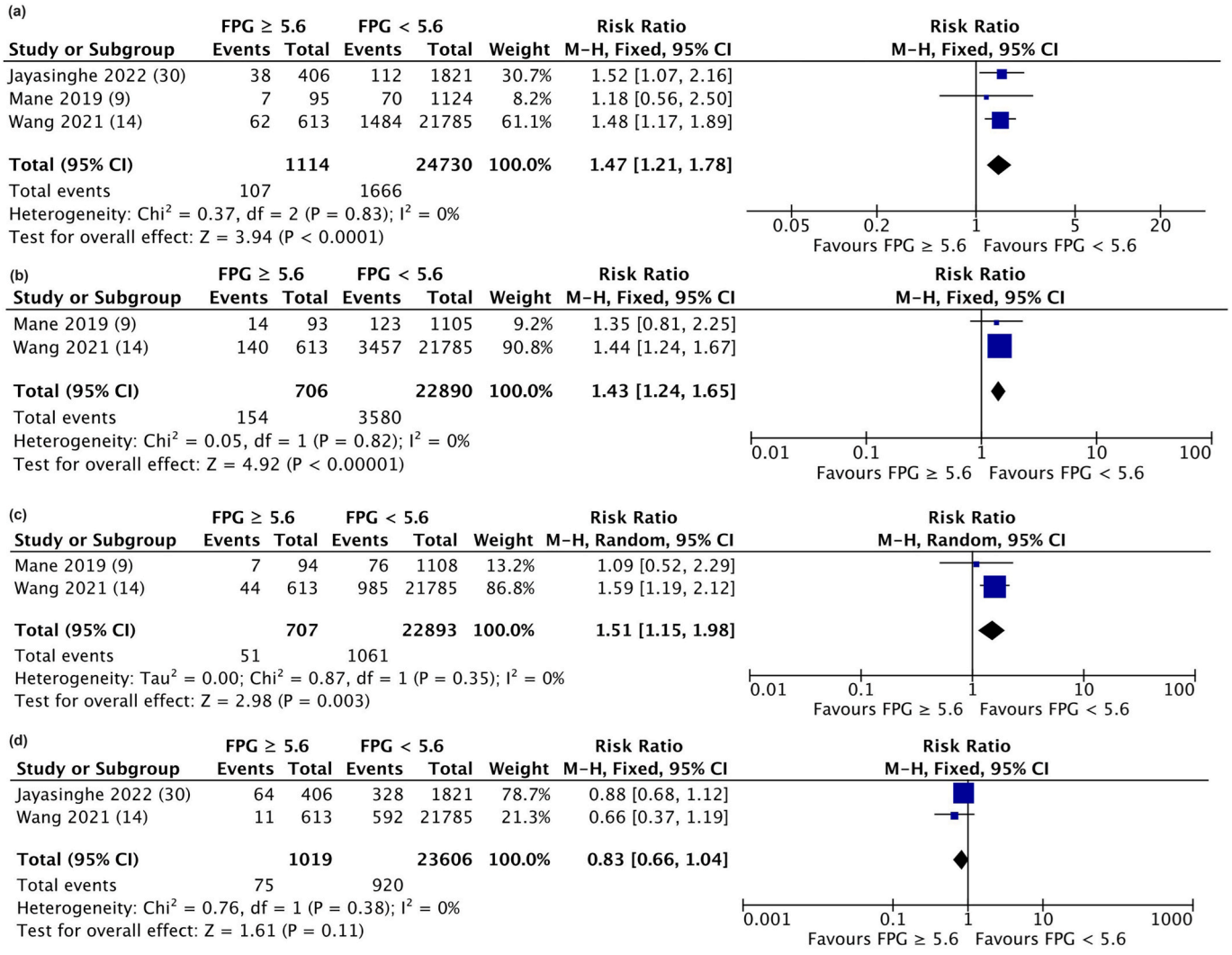

Figure-3. Forest plot highlighting the impact of fasting plasma glucose ≥5.6 mmol/L in the first trimester as compared to controls on the occurrence of (a) macrosomia, (b) large for gestational age, (c) preterm delivery, and (d) small for gestational age. FPG – fasting plasma glucose (value in mmol/L).

We analyzed 11 studies that examined whether first-trimester FPG as a continuous variable below the threshold for diagnosis of overt diabetes is associated with the risk of developing cGDM. Our meta-analysis suggests a linear association between elevated first-trimester FPG and the risk of cGDM with a MD of 0.28 mmol/L (5 mg/dL) between the two groups. A cut-off value, however, could not be derived because of the lack of individual patient-level data in the included studies.

In the study by Riskin-Mashiah et al. [32], a strong graded linear relationship was observed between first-trimester FPG and the development of cGDM. The median first-trimester FPG in women with and without cGDM were 4.3 mmol/L (79 mg/dL) and 4.8 mmol/L (86 mg/dL) respectively. The major limitation of the study was use of FPG >5.8 mmol/L (105 mg/dL) as an exclusion criterion. In the recently published study by Tong et al. [26], retrospective analysis of data from 48,444 pregnancies demonstrated that increased first-trimester FPG, in addition to risk of cGDM, was associated with LSCS, macrosomia, gestational hypertension, and LGA. A linear association between elevated first-trimester FPG and LGA [20,33,34], macrosomia [33], LSCS/assisted vaginal delivery [20,33], and gestational hypertension [21] have been reported. Interestingly, a few studies found that the worsened outcome persisted even in the absence of development of cGDM at 24–28 weeks [15,34].

Despite emerging evidence of a linear risk of development of cGDM and other adverse impacts on pregnancy with rising first trimester FPG, a consensus on a diagnostic threshold for eGDM has not been reached. In our systematic review, an FPG cut-off value of 5.1 mmol/L (92 mg/dL) could predict the development of pre-eclampsia, gestational hypertension, LGA, macrosomia, and cGDM though there was no relationship to rates of preterm delivery, LSCS, SGA, and neonatal hypoglycemia. A diagnostic threshold of 5.6 mmol/L (100 mg/dL) showed an association with LGA, macrosomia, and preterm delivery but not SGA or LSCS. The RR of macrosomia went up from 1.29 to 1.47, and LGA increased from 1.32 to 1.43 as the FPG cut-off changed from 5.1 mmol/L (92 mg/dL) to 5.6 mmol/L (100 mg/dL), underscoring the probability of linearity of the association.

The ADA has recently endorsed an FPG cutoff of 6.1 mmol/L (110 mg/dL) for the diagnosis of early abnormal glucose metabolism, indicating that treatment may be advantageous when levels exceed this threshold [4]. Our literature search, however, revealed only one study assessed this cut-off. An association with pre-eclampsia, LSCS, birth weight >90th percentile, or preterm delivery was not observed above this threshold. However, of the 1228 pregnancies, only 27 had an first-trimester FPG ≥6.1 mmol/L (110 mg/dL), and the number of events was too few for a meaningful analysis [7]. Another study reported a cGDM incidence of 50 % with first-trimester FPG levels between 5.60 mmol/L (100 mg/dL) and 6.1 mmol/L (110 mg/dL). The incidence of cGDM went up to 66.2 % at FPG level ≥6.1 mmol/L (110 mg/dL). The specificity for diagnosis of cGDM was 0.99 and 1 at FPG cut-points of 5.6 mmol/L (100 mg/dL) and 6.1 mmol/L (110 mg/dL), respectively. However, the study did not report findings related to perinatal outcomes [35].

Though our systematic review suggests that the first trimester FPG ≥5.1 mmol/L (92 mg/dL) can predict the development of several adverse gestational outcomes, it is noteworthy that the included studies were observational, and the benefits of commencing treatment at this threshold are unclear. The results of early intervention in women diagnosed with eGDM have been variable. While one study reported benefit [36], others have suggested that early treatment does not alter the outcome [37,38]. The pilot trial of Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) using WHO-OGTT criteria suggested early intervention could decrease the rates of LGA at the cost of increased risk of SGA and fetal undernutrition [39].

The TOBOGM trial was completed recently and the findings suggest that glucose-lowering intervention before 20 weeks led to a significantly lower incidence of a composite of adverse neonatal outcomes. No difference was observed in the other two primary outcomes of pregnancy-related hypertension and neonatal lean body mass. Interestingly, pre-specified subgroup analysis indicate a greater benefit on the composite adverse neonatal outcome in women who underwent OGTT before 14 weeks gestation. Additionally, another subgroup analysis demonstrated a more pronounced effect among women with higher plasma glucose values (high risk group) during OGTT. The FPG criteria used to define higher and lower risk groups were 5.1–5.2 mmoL/l (92–94 mg/dL) and 5.3–6.9 mmol/L (95–125 mg/dL) respectively. Thus, the TOBOGM trial findings implies that early intervention especially in women with higher plasma glucose values could be beneficial [40].

Our meta-analysis has several limitations. Key among them is the significant heterogeneity in design and diagnostic methods among the included studies. Most studies were cohort or case-control in nature, resulting in lower-quality of evidence. Some studies had sampling bias due to targeting high-risk women. Additionally, our review excluded first-trimester interventions, precluding the evaluation of the impact of glucose-lowering therapy on eGDM outcome.

This systematic review is the first to demonstrate a linear increase in the risk of adverse maternal and fetal outcomes with elevated first-trimester FPG. Our findings further reveal that even above an FPG cut-off of 5.2 mmol/L (92 mg/dL) in the first trimester, the risk of cGDM escalates. Therefore, early FPG testing during pregnancy, beyond diagnosing overt diabetes, may aid in identifying individuals needing proactive GDM screening at 24–28 weeks. This approach could be especially relevant in resource-limited settings. However, to fully ascertain the utility and effectiveness of this strategy, further well-designed trials are needed. Our findings also emphasize the need for further research to assess the short-term and long-term impact of early glucose-lowering intervention in pregnant women with FPG levels above 5.2 mmol/L (92 mg/dL).

5. Conclusion

Our meta-analysis indicates that intermediately elevated first-trimester FPG levels increases the likelihood of developing GDM at 24–28 weeks in a linear fashion. Furthermore, our observations have highlighted an increase in adverse perinatal outcomes when FPG levels surpassed 5.1 mmol/L (92 mg/dL) during the initial stages of pregnancy. To ascertain the clinical significance of our findings, it is imperative that appropriately designed trials to assess therapeutic interventions targeting lower first-trimester FPG thresholds be conducted.

Declaration of interest

Saptarshi Bhattacharya, Lakshmi Nagendra, Deep Dutta, Sunetra Mondal, Sowrabha Bhat, John Michael Raj, Hiya Boro, A.B.M. Kamrul-Hasan and Sanjay Kalra have no conflict of interest to declare.

Author contribution

SA.B, L.N and D. D researched data, contributed to discussion, and wrote the first draft of the manuscript. S.M reviewed and edited the manuscript. SO.B, J.R, H·B, A.B.M.K·H and S·K researched data and reviewed and edited the manuscript. All authors approved the final version of the manuscript. L.N is the guarantor for the manuscript.

Prior presentation

No prior presentation of this paper was done.

Disclosures

None for all authors.

Declaration of competing interest

I DR LAKSHMI NAGENDRA WOULD LIKE TO CERTIFY ON BEHALF OF ALL THE CO-AUTHORS AND MYSELF THAT WE HAVE NO CONFLICT OF INTERESTS.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2024.103051.

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