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Review Article

Early Gestational Glucose Intolerance (EGGI): A Comprehensive Review of current evidences and its future directions

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Abstract

Background: Gestational diabetes mellitus (GDM) has traditionally been screened for and diagnosed between 24 and 28 weeks of gestation. Rising rates of obesity, insulin resistance, and first-trimester hyperglycaemia — particularly in South Asian and Indian populations — have driven interest in earlier detection.

Objectives: Early Gestational Diabetes Mellitus (eGDM), typically diagnosed before 20-24 weeks using fasting plasma glucose thresholds, has been increasingly studied, most notably through the multicentre Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) trial.

Methods: More recently, Indian investigators have proposed an even earlier construct — Early Gestational Glucose Intolerance (EGGI) — defined as a postprandial blood glucose (PPBG) of ⩾110 mg/dl detected at 8-10 weeks of gestation, before fetal beta-cell insulin secretion begins around the 10th-11th week. Results: This review synthesizes the physiological rationale, proposed diagnostic criteria, available evidence (including the Diabetes in Pregnancy Study Group India [DIPSI] test, the TOBOGM trial, and Indian hospital-based EGGI cohorts), management strategies centred on Medical Nutrition Therapy (MNT) and metformin, and the current controversies and evidence gaps surrounding EGGI.

Conclusion: While early observational and interventional data suggest that identifying and treating EGGI may reduce composite adverse neonatal outcomes, the concept remains outside mainstream international guidelines, and larger randomized trials are needed before EGGI can be recommended for universal, first-trimester screening.

1. Introduction

Gestational diabetes mellitus (GDM) is conventionally defined as glucose intolerance first recognized during pregnancy. For decades, screening has been anchored at 24-28 weeks of gestation, informed largely by the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, which demonstrated a continuous, graded relationship between maternal glucose levels and adverse outcomes such as macrosomia, caesarean delivery, neonatal adiposity, and elevated cord blood C-peptide. These findings underpinned the International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic thresholds that are now widely used worldwide.

Rationale & Objective of Study: However, a substantial proportion of pregnant women — particularly in South Asia — already display glucose abnormalities well before the traditional

24-28-week window. This observation has given rise to two related but distinct constructs: Early Gestational Diabetes Mellitus (eGDM), generally diagnosed before 20-24 weeks using adapted fasting glucose criteria, and, more recently, Early Gestational Glucose Intolerance (EGGI), a first-trimester (8-10 week) construct proposed by Indian researchers associated with the Diabetes in Pregnancy Study Group India (DIPSI). This review aims to clarify the terminology, present the physiological and epidemiological rationale for early detection, summarize the key evidence base, and outline current management approaches and controversies.

2. Physiology of Glucose Metabolism in Early Pregnancy

Normal pregnancy is characterized by progressive insulin resistance, mediated by placental hormones (human placental lactogen, progesterone, cortisol, and placental growth hormone), which intensifies through the second and third trimesters to ensure nutrient supply to the growing fetus. In the first trimester, however, maternal insulin sensitivity is often relatively preserved or even enhanced, meaning that abnormal glycaemic values detected this early usually reflect pre existing or early-onset metabolic dysfunction rather than pregnancy-induced insulin resistance alone.

A key physiological anchor for the EGGI concept is the timing of fetal pancreatic development: fetal beta-cells begin secreting insulin at approximately 10-11 weeks of gestation. According to the Pedersen hypothesis (and its modern refinements), maternal hyperglycaemia crossing the placenta stimulates fetal beta-cells to secrete excess insulin, resulting in fetal hyperinsulinemia. This, in turn, drives increased fetal adiposity, macrosomia, and — through developmental programming — a higher lifetime risk of obesity, insulin resistance, and type 2 diabetes in the offspring. Proponents of EGGI argue that identifying and correcting maternal hyperglycaemia before the 10th-11th week could interrupt this fetal programming process at its earliest possible point, a strategy sometimes termed 'primordial prevention' of diabetes.

Literature search methodology: All Major databases such as **GOOGLE, PUBMED, SCOPUS** etc were searched on keyword: **Early Gestational Glucose Intolerance, Inclusion Criteria - all studies of any type from last 20 years were included.**

3. GDM to eGDM to EGGI: Evolving Terminology

3.1 Standard GDM

Standard GDM is diagnosed at 24-28 weeks using a 75g OGTT, with diagnosis confirmed if any one of the following IADPSG thresholds is met or exceeded: fasting plasma glucose ⩾92 mg/dl (5.1 mmol/L), 1-hour ⩾180 mg/dl (10.0 mmol/L), or 2-hour ⩾153 mg/dl (8.5 mmol/L). These thresholds were derived from the HAPO study's continuous risk associations, adjusted to an odds ratio of 1.75 for adverse outcomes, adjusted to an odds ratio of 1.75 for adverse outcomes; while the DIPSI Indian Criteria is based on odds ratio of 1.50 with cut off OGCT value ⩾140 mg/dl.

3.2 Early GDM (eGDM) eGDM

refers to glucose intolerance meeting GDM-equivalent criteria but diagnosed earlier than the traditional window — typically before 20 weeks (as in the TOBOGM trial definition) and sometimes up to 24 weeks. The TOBOGM trial enrolled women with risk factors for GDM who met IADPSG criteria at a mean gestational age of 15.6 ± 2.5 weeks, distinguishing eGDM operationally from both standard GDM and overt diabetes in pregnancy (which is excluded via more stringent fasting/2-hour cut-offs).

3.3 Early Gestational Glucose Intolerance (EGGI)

EGGI is a more recently proposed, India-specific construct, distinct from eGDM in both timing and test used. It is defined as a postprandial blood glucose (PPBG) ⩾110 mg/dl on a non-fasting 75g glucose challenge performed at 8-10 weeks of

gestation — i.e., before the 10th–11th week onset of fetal beta-cell insulin secretion. Proponents (Seshiah, Jain, and colleagues, writing through the DIPSI group argue that this cut-off, lower than the standard DIPSI GDM threshold of ⩾140 mg/dl, identifies a sub-diagnostic but clinically actionable degree of glucose intolerance uniquely relevant to the earliest window of fetal metabolic programming. EGGI is explicitly framed as distinct from eGDM: eGDM is diagnosed by fasting glucose criteria at a later (though still early) gestational age, whereas EGGI targets a much earlier, non-fasting, lower threshold intended to precede fetal beta-cell activation.

Table : 01: Comparison of standard GDM, early GDM (eGDM), and the proposed EGGI construct.

Feature	Standard GDM (IADPSG/HAPO)	Early GDM (eGDM / TOBOGM)	EGGI (proposed)
Timing of testing	24–28 weeks	<20–24 weeks (mean ~15.6 wks in TOBOGM)	8–10 weeks (first trimester)
Test used	75g OGTT, fasting	Fasting plasma glucose / 75g OGTT	Non-fasting 75g glucose challenge (DIPSI-type)
Diagnostic threshold	Any 1 of: FPG ≥92, 1h ≥180, 2h ≥153 mg/dl	FPG ≥92–100 mg/dl (varies by guideline)	PPBG ≥110 mg/dl (2-hr, non-fasting)
Rationale	Derived from HAPO continuous-risk data	Detects pre-existing/early insulin resistance	Detects sub-diagnostic glycaemia before fetal beta-cell activation (~10–11 wks)
Clinical action	MNT ± insulin/metformin	MNT ± pharmacotherapy; repeat OGTT at 24–28 wks if not met	MNT ± metformin; serial monitoring through pregnancy

4. Rationale for Early Detection in the South Asian Context

India and other South Asian populations have among the highest global burdens of GDM and type 2 diabetes, attributed in part to the so-called South Asian or 'thin-fat' phenotype. This phenotype is characterized by low birth weight, earlier age of diabetes onset, a lower BMI threshold for metabolic risk, higher insulin resistance and serum insulin levels, more rapid decline in beta-cell function, an atherogenic dyslipidaemia pattern (low HDL, high triglycerides, small dense LDL), low adiponectin, elevated inflammatory markers (hs-CRP, IL-6), reduced muscle mass, increased visceral adiposity, and a higher prevalence of steatotic liver disease. These features predispose Indian women to glucose intolerance manifesting earlier and at lower BMI thresholds than in Western populations, providing part of the rationale for lowering both the gestational age and glycaemic threshold at which screening is initiated.

The Diabetes in Pregnancy Study Group India (DIPSI) has, since the mid-2000s, advocated a single-step, non-fasting 75g oral glucose challenge test (OGCT) as a practical, cost-effective universal screening tool suited to resource-limited settings, avoiding the logistical difficulties of fasting OGTTs (repeat visits, patient discomfort, nausea). The National Institutes of Health (NIH) and DIPSI have further argued that, given fetal beta-cell insulin secretion begins by the 10th 11th week, screening should ideally begin during this window — the physiological basis for the EGGI proposal.

5. Evidence Base

5.1 The HAPO Study and IADPSG Criteria[1-3]

The HAPO study, a prospective observational study of over 25,000 pregnant women across 15 centres, demonstrated strong, continuous associations between maternal glucose levels below the diabetic range and adverse outcomes including large-for-gestational-age infants, neonatal adiposity, elevated cord C-peptide, and caesarean delivery. These findings led directly to the IADPSG diagnostic criteria adopted (with some local modifications) by the WHO, ADA, and most national bodies. Applying IADPSG criteria across HAPO centres yielded an overall GDM frequency of 17.8% (range 9.3–25.5%), highlighting substantial population variation.

5.2 The DIPSI Test — Validation and Limitations[2,3]

Multiple Indian validation studies have compared the DIPSI non-fasting 75g OGCT (2-hour threshold ⩾140 mg/dl) against WHO 1999 and IADPSG criteria. Findings have been mixed: some single-centre South Indian studies reported high concordance (sensitivity and specificity approaching 100%) between DIPSI and the standard fasting 75g OGTT, while larger multi-criteria comparisons (e.g., in Tamil Nadu) found

that DIPSI missed a meaningful proportion of women identified by IADPSG or WHO 1999 criteria, and vice versa. An Italian study directly comparing DIPSI and IADPSG criteria in the same cohort found similar overall prevalence but divergent case identification, underscoring that the two criteria are not interchangeable. DIPSI's principal advantages remain practicality, low cost, and avoidance of fasting related logistical barriers, particularly relevant in high-volume or rural antenatal settings.

5.3 The TOBOGM Trial[4-8]

TOBOGM (Treatment of Booking Gestational Diabetes Mellitus) is the first large multicentre randomized controlled trial directly testing whether treating GDM-equivalent hyperglycaemia diagnosed early in pregnancy (before 20 weeks) improves outcomes compared with deferred treatment until the standard 24-28 week window. Conducted across Australia, Austria, Sweden, and India, TOBOGM randomized 802 women with early GDM (mean gestational age 15.6 ± 2.5 weeks) to immediate versus deferred treatment. The primary composite neonatal outcome (encompassing preterm birth, respiratory distress, macrosomia, birth trauma, shoulder dystocia, and hyperbilirubinemia requiring phototherapy, among others) occurred in 24.9% of the immediate-treatment group versus 30.5% of controls — an absolute risk reduction of 5.6 percentage points. A secondary analysis found a 43% relative reduction in neonatal respiratory distress specifically in the intervention arm, along with a modest reduction in nursery stay. A subsequent economic evaluation found early diagnosis and treatment to be cost-saving (dominant) relative to usual care. Postpartum follow-up of TOBOGM participants also found that roughly one-quarter of women with early GDM had persistent postpartum dysglycaemia, reinforcing the link between early pregnancy hyperglycaemia and future metabolic risk.

5.4 Indian EGGI-Specific Studies[9-17]

The EGGI construct itself has been advanced primarily through a series of Indian & International publications. Seshiah and colleagues (Cureus, 2022) first proposed administering MNT with or without metformin to women with PPBG ⩾110 mg/dl at 8-10 weeks, framing this as prediction and 'primordial prevention' of GDM and its sequelae, rather than treatment of an already-established diagnosis. This was followed by a formal description of the EGGI concept (Seshiah et al., Diabetes Asia Journal, 2024), explicitly distinguishing EGGI from eGDM and advocating universal EGGI screening by the 10th week using the ⩾110 mg/dl threshold

A hospital-based prospective cohort study conducted at the Upper India Sugar Exchange Maternity Hospital, Kanpur (Verma, Agarwal, Gupta, Jain, Seshiah, and colleagues, 2025), enrolled 231 pregnant women at 8–10 weeks with PPBG ⩾110 mg/dl, comparing MNT alone against MNT combined with metformin. Women receiving MNT plus metformin showed significantly lower mean PPBG at every follow-up point (12, 16, 24, and 32 weeks) than those on MNT alone, and a significantly lower rate of composite adverse neonatal outcomes (17.1% versus 32.4%, p ⩽ 0.0001). Table 2 summarizes these findings..

Table 2. Key glycaemic and neonatal outcomes from the Kanpur EGGI cohort study (n = 231).

Outcome (Kanpur EGGI cohort, n=231)	MNT alone	MNT + Metformin	P-value
Mean PPBG at 12 weeks (mg/dl)	134.1 ± 10.7	126.8 ± 6.6	≤0.001
Mean PPBG at 16 weeks (mg/dl)	126.7 ± 13.2	123.0 ± 8.5	≤0.001
Mean PPBG at 24 weeks (mg/dl)	124.8 ± 11.0	117.8 ± 4.9	≤0.001
Mean PPBG at 32 weeks (mg/dl)	127.7 ± 17.7	113.9 ± 8.9	≤0.001
Composite adverse neonatal outcome	32.4% (35/108)	17.1% (21/123)	≤0.0001

A related earlier report (Tiwari, Agarwal, Jain, Seshiah, et al., 2024[9-14) similarly found that metformin treatment for early gestational glucose intolerance reduced primary neonatal outcomes in a hospital-based cohort, consistent with the later, larger Kanpur dataset. Together, these studies constitute the primary observational and quasi-experimental evidence base specific to the EGGI construct, though none yet constitutes a large, multi-centre, blinded randomized controlled trial of EGGI treatment itself.

6. Management of EGGI[18-27]

6.1 Medical Nutrition Therapy (MNT)

MNTremains the cornerstone of management for any degree of gestational glucose intolerance, including EGGI. Individualized dietary counselling — emphasizing appropriate caloric intake, complex carbohydrates with a low glycaemic index, adequate protein, fibre, and controlled portion sizes across small, frequent meals — aims to limit postprandial glycaemic excursions while supporting fetal growth. In the Indian EGGI literature, MNT is typically initiated at the time of diagnosis (8–10 weeks) and continued throughout pregnancy, with or without adjunctive pharmacotherapy, depending on response.

6.2 Metformin in Early Pregnancy

Metformin, an insulin-sensitizing biguanide, has an expanding evidence base in pregnancy. It is not a controlled substance and, unlike insulin, does not require injection, refrigeration, or titration by a diabetes educator, making it attractive for early, potentially transient glycaemic abnormalities. Register-based cohort data have not shown consistent adverse long term outcomes in metformin-exposed pregnancies, and metformin is already widely used later in pregnancy for confirmed GDM as an alternative or adjunct to insulin. A randomized trial of early metformin specifically in women already diagnosed with GDM, Dunne et al., JAMA 2023[23]) found that metformin reduced the composite need for insulin initiation or elevated fasting glucose later in pregnancy, supporting a broader role for early pharmacological intervention in glucose-intolerant pregnancies. Nonetheless, metformin crosses the placenta, and long-term offspring outcomes (metabolic programming effects of transplacental metformin exposure) remain an area of ongoing research and some caution, particularly given the theoretical possibility of effects on fetal AMPK-mediated metabolic pathways.

6.3 Monitoring and Follow-Up

Where EGGI is identified and treated, protocols described in the Indian literature involve serial PPBG monitoring at approximately 12, 16, 24, and 32 weeks of gestation, alongside standard antenatal surveillance for fetal growth (serial ultrasound biometry), and repeat formal GDM testing at 24–28 weeks per usual practice, since EGGI at 8–10 weeks does not replace, but precedes and supplements, standard-interval screening. A multidisciplinary team — obstetrician, diabetologist/physician, dietitian, and diabetes educator — is recommended, consistent with broader DIPSI and FIGO guidance on GDM care models.

7. Maternal and Neonatal Outcomes

The available EGGI-specific and eGDM evidence converges on a consistent signal: earlier identification and treatment of gestational hyperglycaemia is associated with reduced composite adverse neonatal outcomes, including reductions in respiratory distress, macrosomia, birth trauma, and shorter nursery stays, without a demonstrated increase in adverse outcomes such as small-for-gestational-age births in the treated groups reported to date. The addition of metformin to MNT in the Kanpur EGGI cohort nearly halved the rate of composite adverse neonatal outcomes compared to MNT alone. However, it should be emphasized that most EGGI-specific data derive from few centres in india, non-blinded, and randomized cohorts [28,29,30], whereas the TOBOGM trial — though methodologically the strongest evidence for early treatment — tested a somewhat different, later (mean ~15.6 weeks) and fasting-glucose-based definition (eGDM), not the 8–10-week, non-fasting EGGI definition specifically.

8. Controversies and Evidence Gaps

- Terminological ambiguity: EGGI, eGDM, and 'gestational glucose intolerance' (GGI, as used by some Western authors to denote an abnormal screening test without a formal GDM diagnosis) are sometimes used loosely or inconsistently across the literature, risking confusion in both clinical practice and research synthesis.
- Not established as an independent risk factor everywhere: a large US retrospective cohort (Selen et al., Diabetes Care, 2023[22]) found

that gestational glucose intolerance (an abnormal initial screen without a formal GDM diagnosis) was not, in that population, a recognized independent risk factor for future diabetes — a finding that cautions against over-interpreting any single abnormal early glucose value as inherently pathological.

- Diagnostic threshold variability: first-trimester fasting glucose thresholds for eGDM perform poorly at predicting later-diagnosed GDM and likely need population-specific recalibration by ethnicity, gestational age, and BMI, a concern that may also apply to the EGGI PPBG ⩾110 mg/dl threshold, which has not yet been validated against long-term hard outcomes in large, diverse cohorts.
- Limited external validation: the EGGI construct and its ⩾110 mg/dl cut-off originate from a small number of Indian research groups and a single major hospital-based cohort; it has not yet been adopted or replicated by international bodies (ADA, WHO, IADPSG, FIGO), nor tested in large, adequately powered, randomized, multi centre trials designed specifically around the EGGI definition.
- Risk of overdiagnosis and overtreatment: universal first-trimester screening at a lower threshold than standard GDM criteria will inevitably increase the number of women labelled with a glycaemic abnormality, with attendant psychological, resource, and medicalization costs, particularly if a meaningful proportion would have normalized spontaneously as pregnancy progressed.

9. Future Directions

Several steps could strengthen the evidence base and clinical utility of the EGGI concept:

- Large, adequately powered, multi-centre randomized controlled trials specifically testing the EGGI definition (8 10-week, non-fasting PPBG ⩾110 mg/dl) against deferred/standard-interval screening, with pre-specified long term maternal and offspring outcomes.
- Population-specific threshold validation studies across diverse ethnic groups, BMI categories, and healthcare settings, rather than extrapolation from single-population cohorts.
- Long-term offspring follow-up studies (metabolic, anthropometric, neurodevelopmental) for pregnancies exposed to first-trimester metformin.
- Formal cost-effectiveness and health-system feasibility analyses of universal first-trimester screening in varied resource settings, building on the cost-effectiveness precedent established for eGDM by the TOBOGM economic evaluation.
- Efforts toward international terminological consensus to clearly differentiate EGGI, eGDM, and GGI in future guideline documents and research reporting.
- Metformin's long-term offspring safety: while short/medium-term data are reassuring, transplacental metformin exposure in the first trimester — the period of major organogenesis — has a comparatively smaller evidence base than its use later in pregnancy, and long-term metabolic outcomes in exposed offspring warrant continued follow up.

10. Conclusion

Early Gestational Glucose Intolerance (EGGI) represents an evolving, physiologically grounded proposal to shift the window of gestational glycaemic screening from the traditional 24–28 weeks to as early as 8–10 weeks, anchored to the onset of fetal beta-cell insulin secretion. Emerging Indian cohort data, including a substantial hospital-based study from Kanpur, suggest that identifying and managing EGGI with MNT and metformin may meaningfully reduce composite adverse neonatal outcomes. These findings are complementary to, but methodologically distinct from, the stronger randomized-trial evidence supporting treatment of early GDM (eGDM) in the TOBOGM trial. At present, EGGI remains a promising but not yet

internationally validated construct; its adoption into routine, universal first-trimester screening should await larger, multi-centre randomized trials, population-specific threshold validation, and longer-term offspring safety data, particularly regarding early metformin exposure.

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Note: This review is intended for academic and educational purposes. It synthesizes currently available literature on EGGI, a relatively new and evolving concept; readers should consult sources and current professional guidelines before applying any diagnostic threshold or treatment protocol in clinical practice.

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