

## INPLASY

## A Systematic Review on Biomarkers for Gestational Diabetes Mellitus Detection in ART Pregnancies: Current Trends and Future Directions

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**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Risk of bias assessment.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202550080**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 May 2025 and was last updated on 27 May 2025.**INTRODUCTION**

**Review question / Objective** Gestational diabetes mellitus (GDM) is a frequently encountered medical complication during pregnancy that is increasing at a rapid pace globally, posing significant public health concerns. Similarly, there is a rising trend in the number of women who have undergone assisted reproductive technology (ART). Numerous studies have been carried out to investigate the relationship between GDM and ART. This comprehensive systematic review seeks to identify potential biomarkers for the early diagnosis of GDM in pregnancies conceived through ART.

**Rationale** We conducted a PubMed search covering the past five years to identify studies that explore biomarkers associated with the development of GDM in pregnancies conceived through ART. The outcome measures included HCG, BMI, FSH/LH ratio, increased haemoglobin A1c levels, fasting insulin concentrations, homeostatic model assessment of insulin

resistance (HOMA-IR), triglyceride levels, total cholesterol levels, low-density lipoprotein cholesterol concentrations, LDL/HDL, TC/HDL, estradiol/follicle ratio, sFlt-1, PLGF, endometrial thickness and psychological stress.

**Condition being studied** The incidence of pregnancies resulting from ART is steadily rising globally. Consequently, increasing attention has been directed towards the potential risks as a result of ART. At present, evidence suggests that women who achieve pregnancy via ART may face a higher risk of adverse outcomes compared to those who conceive naturally. GDM has been linked to an increased likelihood of preeclampsia and caesarean delivery in mothers, as well as macrosomia, hypoglycemia, shoulder dystocia, and jaundice in newborns. Advanced maternal age, polycystic ovary syndrome (PCOS), multiple pregnancies, and obesity are key risk factors for GDM. These factors are also commonly observed in women who have undergone ART, indicating a possible link between ART and an increased risk of GDM.

The potential link between GDM and ART has been the subject of extensive investigation in numerous studies.

This review aimed to integrate the most reliable evidence available on the availability of biomarkers for assessing the increased likelihood of GDM among singleton gestations resulting from in vitro fertilization (IVF).

## METHODS

**Search strategy** A literature search in MEDLINE was conducted independently by two reviewers, covering the past five years. The present review adhered to the PRISMA guidelines for systematic reviews and meta-analyses.

**Participant or population** Population—singleton pregnancies.

**Intervention** Intervention—assisted reproductive technologies (ART).

**Comparator** Comparator—gestational diabetes mellitus (GDM) versus normoglycaemic pregnancies.

**Study designs to be included** Systematic Review.

**Eligibility criteria** The inclusion criteria were established prior to the commencement of the literature search and were as follows:

- i) comparative evidence on the incidence of GDM in women who achieved a singleton pregnancy through ART.
- (ii) Only full-text, peer-reviewed articles
- (iii) Studies of any design published within the last five years
- (iv) Articles written in English
- (v) Availability of an abstract.

**Information sources** PubMed/Medline.

**Main outcome(s)** Outcome—biomarkers..

**Quality assessment / Risk of bias analysis** A formal quality assessment using the Newcastle-Ottawa Scale was performed.

**Strategy of data synthesis** Combining and evaluating data extracted from individual studies to create a coherent understanding of the research question.

**Subgroup analysis** Not performed.

**Sensitivity analysis** Not performed.

**Country(ies) involved** Greece.

**Keywords** Assisted Reproductive Technology; Gestational Diabetes Mellitus; IVF; ICSI; Biomarker.

## Contributions of each author

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