



# The association between COVID-19 and gestational diabetes mellitus: A narrative review

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## Abstract

The outbreak of COVID-19 has become an important health concern with diverse complications. Based on previous studies, women with gestational diabetes mellitus (GDM) are at a higher risk of COVID-19. Although numerous investigations have assessed the epidemiological and clinical aspects of this virus in pregnancy, few articles have clearly emphasized the role of COVID-19 in increasing the risk of GDM. In this narrative review, we aimed to assess the relationship between COVID-19 and GDM.

**Keywords:** Coronavirus, COVID-19, Diabetes, Pregnancy

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## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a new coronavirus, was first introduced in Wuhan, China, in 2019 and immediately became a pandemic. Coronavirus disease 2019 (COVID-19) has been diagnosed in 529 410 287 million people worldwide, with 6 296 771 million deaths by June 2022 (1). Pregnant women are high-risk patients and should be comprehensively under control. With the simultaneous occurrence of gestational diabetes mellitus (GDM) and coronavirus, they would be more vulnerable (2).

Gestational diabetes mellitus has negative child and maternal outcomes such as hypertension, cardiovascular disease, hypoxia, preeclampsia, neonatal hypoglycemia, macrosomia, and type 2 diabetes (3-5).

As more scientific and clinical research is required to assess the association between COVID-19 and GDM to find the best way to manage and diagnose it, we aimed to perform this narrative review.

## Methods

We assessed the potential relationship between COVID-19 and GDM in this narrative review. We searched and extracted relevant English publications from the Web of Science, Scopus, PubMed, and Google Scholar using specific keywords including GDM, COVID-19, pregnancy, and Gestational diabetes. We attempted to find the relationship between COVID-19 and GDM.

Furthermore, we discussed the diagnosis and management of COVID-19 patients with the criteria of GDM.

## The outbreak of COVID-19

Reports on a cluster of unknown causes of pneumonia in China in December 2019 led to the discovery of a new coronavirus in 2020. It was labeled as COVID-19 (6). It quickly spread globally, forcing the World Health Organization (WHO) to announce it a pandemic in March 2020, prompting several countries to take extraordinary public health measures to stop it. By May 2022, approximately 500 million confirmed cases and over 6 million deaths had been reported (1).

Clinical characteristics of COVID-19 ranging from asymptomatic to critical are as follows (7);

- Asymptomatic: Without symptoms and findings in chest imaging
- Mild: Mild symptoms (including fatigue, fever, cough, muscle pain, anorexia, sore throat, headache, malaise, dyspnea, nasal congestion) without abnormal findings on chest imaging
- Moderate: Mild or moderate symptoms with mild pneumonia abnormalities on chest imaging
- Severe: symptoms of respiratory infection and some of the following features: oxygen saturation  $\leq 93\%$  at rest,  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mm Hg,  $\text{RR} \geq 30$  breaths/min, shortness of breath
- Critical: Rapid disease progression and some of the

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following features: Shock, Mechanical ventilation due to respiratory failure, necessitates ICU treatment, and organ failure.

### Gestational diabetes mellitus

Gestational diabetes mellitus initially occurs or detects in case of glucose intolerance or diabetes during pregnancy. It is known as one of the causes of infant and maternal mortality (8). Additionally, it is a serious health problem that affects one out of every six births worldwide (9).

Physiologically, insulin requirements rise during pregnancy. Several factors contribute to insulin demand increment, including raised maternal caloric intake or weight gain, placental hormones, increased prolactin, and growth hormone secretion. As the pregnancy progresses, the pancreatic  $\beta$ -cell mass grows to meet the increased need for insulin. The  $\beta$ -cell expansion failure causes GDM with a relatively inadequate insulin secretion increase (10).

Pregnant women suffer from hyperglycemia in around 16% of births. The diagnostic criteria and screening approaches demonstrated that the global prevalence of GDM ranged from 2.1% to 37.5% (11).

The risk of GDM progression rises in various situations, including having age over 25 years, having GDM since the last pregnancy, and having a history of type 2 diabetes mellitus or polycystic ovary syndrome (12). Although the cause of GDM is unknown, obesity has been linked to increased maternal age. Women of certain ethnic groups have been reported to be at a higher risk (13).

The GDM diagnosis was established using a one-step method due to the International Association of Diabetes in Pregnancy Study Groups (IADPSG) guideline. Except for high-risk women, who were evaluated at the first prenatal appointment, all pregnant women received 75 g of glucose between 24 and 28 weeks. The oral glucose tolerance was evaluated after two hours. The GDM can be diagnosed if at least one plasma glucose concentration matches or surpasses the guideline thresholds: fasting, 92 mg/dL; 1 hour, 180 mg/dL; or 2 hours, 153 mg/dL. Once women were diagnosed with GDM, they were instructed to change their lifestyle, diet, and nutrition. Additionally, they were told to use glucose meters to check their blood sugar regularly. If the management failed to control a fasting glucose level of 95 mg/dL and a 1-hour postprandial level of 140 mg/dL (or a 2-hour postprandial level of 120 mg/dL), insulin therapy was recommended (14).

### COVID-19 and GDM

The world has been turned upside-down by the COVID-19 outbreak. This issue will hurt the medical profession, especially regarding diabetes diagnosis and management. Moreover, a diabetic epidemic is more likely to occur because of this situation. It is expected that the prevalence of diabetes will increase from 463 million in 2019 to 700 million in 2045. The prevalence of hyperglycemia in pregnancy aged from 20 to 49 years was estimated to

### ■ Implication for health policy/practice/research/medical education

In this narrative review, we attempted to find the relationship between COVID-19 and GDM based on previous studies, women with gestational diabetes mellitus (GDM) are at a higher risk of COVID-19. Moreover, we discussed the diagnosis and management of COVID-19 patients with the criteria of GDM.

be 20.4 million, or 15.8% of all live births in 2019. They reported hyperglycemia in pregnancy, corresponding to GDM in 83.6 percent of cases. As a result, all women should be checked for GDM even if no symptoms present (15).

A study suggested that diabetes mellitus (DM) and obesity or overweight were more common in women diagnosed with COVID-19 during pregnancy than in women not diagnosed with COVID-19 during pregnancy. This issue shows that these risk factors increase the chances of infection. Besides, the COVID-19 disease was related to GDM in women who used insulin (16).

The general understanding is that pregnant women are no more vulnerable than the general population to contracting the coronavirus infection. While women during pregnancy are not necessarily more susceptible to viral disease, their immune systems are influenced by pregnancy-related physiological changes, leading to more severe symptoms, especially in the third trimester (17).

### Diagnosis of GDM during COVID-19

In general, two methods are approved by the IADPSG for GDM screening. A fasting patient takes a 2-hour, 75-g oral glucose tolerance test in the one-step procedure. If one of the glucose results (fasting, after one, or two hours) exceeds the threshold, the result is considered "abnormal" (14).

The "one-step" strategy is the primary approach for diagnosing GDM, and most guidelines recommend this strategy. All around the world, universal GDM screening for all pregnant women is desirable, even during the COVID-19 pandemic. Although it may be more expensive initially, the data show its cost-benefit in the long run. Indeed, type 2 diabetes could be prevented by taking preventative steps and its accompanying cardiovascular consequences, improving the general population's health. All women diagnosed with GDM should be evaluated for glucose intolerance six weeks after postpartum. If fasting plasma glucose is less than 5.6 mmol/dl, she has impaired fasting glucose, and if 2 hours post glucose is less than 7.8 mmol/d, she has impaired glucose tolerance (18).

### GDM management during the COVID-19

Protein is important nutrition and one of the COVID-19 prevention methods. It is critical for immunity like white blood cells, which are the first line of defense against infection and prevent its spreading throughout the body.

During pregnancy, 1.1 g/kg of daily protein is required, equating to 60-70 g of protein. In pregnant women and those with GDM, a balanced meal emphasizing whole pulses, fish, eggs, fruits, and vegetables offers the necessary nutrients to avoid COVID-19 infection (19). There is currently no specific drug available to treat COVID-19 disease.

A review study suggested that herbal medicines such as turmeric, garlic, and ginger were effective treatments for COVID-19, reducing the length of hospital stay, symptoms, and complications of coronavirus infection due to their antiviral effects (20).

Metformin or insulin treatment is the standard management in women with GDM, which is not managed by medical nutrition therapy, even though the first choice is insulin. Insulin therapy would begin at any point. In GDM, 0.1 unit/kg per day is the recommended beginning insulin dosage. The dosage can be raised on follow-up until 2-hour postprandial plasma glucose is about 6.7 mmol/dL (19). Before delivery, every pregnant should be checked for COVID-19. The insulin dosage must be raised if the steroid is necessary for fetal lung maturity or COVID-19.

Metformin should be maintained in an infected pregnant woman with hyperglycemia. Indeed, it is a palliative against every infection until acute problems, including renal failure, ketoacidosis, and respiratory failure. Metformin has a starting dosage of 500 mg twice daily orally with a maximum dose of 2 g/d. If the blood sugar level is not controlled with the highest amount of metformin (2 g/d) and medical nutrition therapy, insulin should be given (19). In this case, COVID-19-positive women will require increased insulin dosage since the infections affect glycemic control through their effect on  $\beta$ -cells.

If a GDM postpartum blood glucose is less than 7.8 mmol/dL, she may be encouraged to continue taking metformin. Metformin is safe to use while breastfeeding. Breastfeeding should be continued for 2 to 6 months to prevent diabetes in both the mother and child (19).

Monitoring the disease and its complications requires daily blood glucose testing, frequent injections, regular clinician appointments, and a healthy lifestyle approach (15). Social distancing, appropriate use of personal protection equipment, and telemedicine are considered to provide clinical services for these individuals to prevent the complications of COVID-19 during pregnancy, including preeclampsia, increased cesarean section, preterm birth, and perinatal death (21, 22).

Moreover, self-care is critical for controlling and treating these patients. It is a collection of self-stimulation acts in which someone is responsible for their health and well-being (15).

Glycated hemoglobin (HbA1c), thyroid and renal function evaluation, and the urine protein to creatinine ratio should be measured at the initial visit of pregnant

women with diabetes. Face-to-face contact is supposed to be kept to a minimum state. If required, schedule in advance with necessary tests and ultrasound sessions at 11–14 weeks, 28–32 weeks, and 34–36 weeks of pregnancy.

The oral glucose tolerance test is not suggested in patients with GDM due to more time at medical centers and limited resources. However, screening with random plasma glucose and HbA1c testing is recommended. In addition, screening after delivery might be postponed for three to six months after birth (23).

## Conclusion

Although glucose metabolism disorders and GDM in pregnancy have been studied extensively during the COVID-19 pandemic, most elements of the subject for diagnosis and treatment remain contentious. One of the primary purposes of this review study was to evaluate previous research and current global guidelines on GDM and analyze the implications of their suggestions during the COVID-19 pandemic. Following a diagnosis of GDM, extra prenatal visits and fetal monitoring are tailored to the maternal glucose control and treatment needs. The COVID-19 outbreak has forced everyone to provide simple answers to every difficulty. If a pregnant woman's diet and lifestyle changes do not work, she may be prescribed metformin or insulin.

## Authors' contribution

Conceptualization: AHR and AFY. Methodology: AHR and AFY. Validation: AHR and AFY. Formal Analysis: AHR and AFY. Investigation: AHR and AFY. Resources: AHR and AFY. Data Curation: AHR and AFY. Writing—Original Draft Preparation: AHR and AFY. Writing—Review and Editing: AHR and AFY. Supervision: AHR and AFY. Project Administration: AHR and AFY.

## Conflicts of interest

The authors declared no conflict of interest.

## Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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