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# Recent overview on medication for Gestational Diabetes

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**Abstract**
Gestational diabetes mellitus (GDM) is a common complication of pregnancy, characterized by glucose intolerance that develops during gestation. Effective management is crucial to prevent adverse maternal and fetal outcomes. This review highlights the recent advancements and current approaches to pharmacological interventions in GDM. Traditionally, Insulin therapy remains the gold standard for uncontrolled hyperglycaemia due to its safety profile and efficacy. However, recent studies have explored the role of Oral Antihyperglycemic agents, such as Metformin and Glyburide, as alternatives or adjuncts to Insulin therapy. Metformin, despite its placental transfer, has shown favourable maternal outcomes, although long-term effects on offspring remain under investigation. Glyburide provides convenience as an oral agent but may increase neonatal hypoglycaemia risk compared to insulin. Emerging evidence also suggests the potential for novel agents and personalized therapy strategies based on genetic and metabolic profiling. This review will be helps to underscores the need for further clinical investigations to establish clear guidelines and ensure the safety and efficacy of newer therapies.

**Keywords:** Gestational diabetes, insulin therapy, metformin, glyburide, pharmacological management, maternal outcomes

## Introduction

Insulin resistance (IR) and hyperinsulinemia are linked to pregnancy and may put certain women at risk for developing diabetes. One Any level of glucose intolerance, in varying degrees of severity, that begins or is observed during pregnancy is known as gestational diabetes mellitus (GDM).2. Pregnant women who were more likely to develop type 2 diabetes mellitus (DM2) after giving birth were identified using GDM fifty years ago. At the moment, index pregnancy morbidity is predicted using GDM. Pregnant women with diabetes mellitus who experience severe hyperglycaemias from the beginning of their pregnancy are more likely to experience detrimental consequences than those who experience mild hyperglycaemias in the latter stages of their pregnancy [1].

One common metabolic issue that is a major concern is gestational diabetes mellitus. The diagnostics are crucial because of this. Although the diagnostic procedures for GDM were initially outlined forty years ago, no one screening technique satisfies worldwide requirements. The difficulty of adopting such a method has been recognized and discussed for years due to the high demand for consistency in the diagnosis and classification of GDM. Until recently, most of the tests employed were on determining the likelihood of acquiring diabetes later in life. pregnancy and not on GDM's perinatal consequences [2].

**Table 1:** potential risk to the fetus in GDM sufferers [1].

| Pregnancy | Early IUGR, congenital deformity, and spontaneous abortion |
|---|---|
| **Second Trimester** | CNS developmental delay and macrosomia |
| **Third Trimester** | Stillbirth, IUD, IUGR, and chronic hypoxemia |
| **During labour** | injuries from birth and shoulder dystocia. |
| **Newborn** | Myocardial dysfunction, respiratory distress syndrome, hypoglycaemia, hypocalcaemia, thrombocytopenia, polycythaemias, hyperbilirubinemia, and renal vein thrombosis |
| **Child and adult** | Birth trauma, behavioral abnormalities, intellectual deficiencies, obesity, and diabetes |

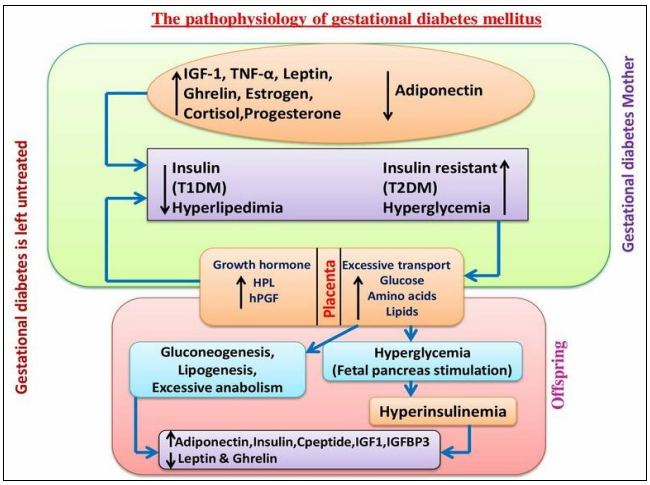


**Fig 1:** Pathogenic factors underlying GDM. As woman gains weight and reduces physical activity during pregnancy, peripheral insulin resistance develops and glucose intoner ance may occur. This in turn undermines pancreatic β-cell function and may contribute to the increased risk of GDM [2]

**Table 2:** Types of diabetes mellitus [2]

| **Type 1** | **Type2** | **Type3** | **Type4** |
|---|---|---|---|
| Insulin Dependent Pancreatic Cell Dysfunction Average age < 30 | Not reliant on insulin Appears more commonly in adults >40 –obesity positive family – insulin resistant | Gestational | Diabetes mellitus secondary to another disease or drug treatment |

## Gestational diabetes mellitus (GDM)

Obesity and overweight from pregnancy, advanced age at maturity, and a prior personal or family history of diabetes in any form are the primary causes. Birth difficulties, abnormal glucose metabolism, and cardiovascular disorders in both the mother and the child are among the long-term risk factors linked to GDM. GDM is mostly treated with dietary and exercise modifications. Additionally, insulin, glibenclamide, and metformin are used to control hyperglycaemias [4].

**Table 2:** Classification of Diabetes by Risk/outcomes [3]

| Pregestational diabetes (10%) | Gestational diabetes (90%) |
|---|---|
| Maternal diabetes type (type 1 or type 2) | Fetal risks |
| Timing and metabolic regulation (early or late pregnancy) | Neonatal risks |
| problems with the mother's blood vessels (retinopathy, nephropathy, and/or atherosclerosis) | Maternal risks |

**Table 3:** Fig 2 Risk factors for gestational diabetes mellitus [3]

| Modifiable factors | Unmodifiable factors |
|---|---|
| High BMI prior to pregnancy<br>Low-quality food<br>A sedentary way of living<br>Lack of vitamin D<br>PCOS elevated levels of total bile acid during the first trimesters. | Advanced maternal age Personal history of GDM or prediabetes Family history of diabetes Ethnicity (Asian, Hispanic, Native American, and African American) Maternal history of low birth weight Low stature Twin pregnancy Genetic susceptibility |

**Table 4:** Diagnostic criteria for overt diabetes and gestational diabetes using a 2-hour 75-g OGTT at 24 to 28 weeks gestational [2]
Diagnosis of GDM

| Diagnosis | Fasting Plasma Glucose, mg/dL | 1-h Value mg/dL | 2-h Value Mg/dl |
|---|---|---|---|
| Overt diabetes (type 1, type 2, or other) | ≥126 mg/dL | Not applicable. | ≥200 mg/dL |
| Gestational diabetes | ≥92 mg/dL | ≥180 mg/dL | ≥153 mg/dL |

**Current GDM Diagnostic Criteria**

Given the rising baseline rates of type 2 diabetes, obesity, and impaired glucose tolerance among young adults and women of reproductive age, it is critical to take into account the rise in GDM prevalence linked to the IADPSG diagnostic criteria. Nearly 18% of HAPO trial participants, for instance, would have satisfied the IADPSG diagnostic criteria for GDM. In contrast, over 29% of US people between the ages of 20 and 44 have prediabetes [5, 6].

**Screening**

The final theme dealt with the experiences of taking the GDM screening exam. The participant's satisfaction with the screening procedure was mostly determined by factors affecting their access to testing. Obtaining childcare, the laboratory's awkward location, scheduling time off work, and transportation issues were among the logistical obstacles. Distaste or aversion to the sugar beverage given, trouble scheduling fasting periods prior to the test, nausea or vomiting, and discomfort with in-person evaluation during the COVID-19 pandemic were among the individual reactions and experiences that caused obstacles [7].

The study population, which consists of mostly Black, non-privately insured individuals from a mid-sized Midwestern city in a state that has not yet extended its Medicaid program, has previously received little attention. Furthermore, a deeper comprehension of the variables influencing long-term outcomes outside of the immediate postpartum period is made possible by the inclusion of people who were both within and beyond a year of birth [8].

According to a recent randomized controlled trial, perinatal outcomes are not improved by early gestational diabetes mellitus (GDM) screening in people who are obese (body mass index [BMI] ≥30 kg/m2) [9].

**Management**

**Lifestyle and Behavioural Management**

- A blood glucose level of less than 95 mg/dL (5.3 mmol/L) and either
- A postprandial glucose level of less than 140 mg/dL (7.8 mmol/L) at one hour or
- A postprandial glucose level of less than 120 mg/dL (6.7 mmol/L) at two hours

Insulin-treated GDM is subject to the same glycaemic target lower limits as preexisting diabetes. Studies indicate that 70–85% of individuals with GDM diagnosed using Carpenter-Clouston criteria can control their condition with lifestyle changes alone, depending on the population. If the lower International Association of the Diabetes and Pregnancy Study Groups (60) diagnostic thresholds are applied, this percentage is expected to be even higher [10].

**Medical Nutrition Therapy**

An RD/RDN experienced in managing GDM works with the lady to create a personalized nutrition plan as part of medical nutrition therapy for GDM. According to 2009 Institute of Medicine guidelines, the diet plan should provide enough calories to support weight gain, attain glycaemic targets, and support maternal, Fetal, and newborn health There is no conclusive study that suggests pregnant women with GDM have different calorie requirements than pregnant women without GDM, or that there is a specific ideal calorie intake for these women [13].

Currently, 175 g, or 35% of 2,000-calorie diets the recommended daily intake of carbohydrates. In addition to lowering free fatty acids, improving insulin action, and improving vascular advantages, liberalizing higher-quality, nutrient-dense carbs may also lessen excess baby adiposity. And could lessen excessive baby fat. When mothers replace carbohydrates with fat, they may inadvertently increase lipolysis, increase free fatty acids, and exacerbate insulin resistance in the mother [11].

**Physical Activity**

A systematic study showed that an exercise intervention improved glucose management and decreased the need to start insulin or the amount of insulin needed. Exercise length (20–50 minutes per day, 2–7 days per week of moderate-intensity) and the types of effective exercise (aerobic, resistance, or both) varied [12].

**Medicine and treatment**

**Treatment satisfaction**

Two quantitative studies and the mixed-methods research both reported treatment satisfaction as a metric. Two studies measured satisfaction using the Diabetes Treatment

Satisfaction Questionnaire (DTSQ). Using a specially created tool, Anderberg *et al*.'s study discovered that 89% of women with GDM were "satisfied," 2% were "neutral," and none expressed discontent. In the Hussain *et al*. study, which employed the DTSQ, 122 (73.5%) of the patients said they were happy with their therapy, but 44 were not; in other words, most patients were happy with their treatment but continued to have a "negative" attitude regarding GDM [14].

**Diet prescribed**

A major contributing factor to the unpleasant experience was the challenge of adhering to a new diet while pregnant, in addition to pragmatic factors like having easy access to fresh food in isolated locations. Negative experiences with handling the recommendations in conjunction with culturally-based diets have been documented in studies with multicultural communities. According to the two studies conducted by Bandyopadhyay, women found it challenging to stick to their traditional diet because of the additional restrictions [15].

**Medication prescribed**

**Insulin**

For the treatment of type 1 diabetes, type 2 diabetes, and uncontrolled gestational diabetes, insulin continues to be the gold standard. Reducing adverse Fetal outcomes, such as anatomical abnormalities, macrosomia, neonatal hypoglycaemia, adolescent and adult obesity, and diabetes, requires strict supervision during the first trimester and throughout pregnancy. Since there is no information on the use of new insulin formulations and strengths in human pregnancy, it is crucial to comprehend them in order to evaluate risks [16].

**Short-Acting Insulin and Rapid-Acting Insulin**

Escherichia coli bacteria produce regular (U-100) insulin, which is the same as human insulin. It is used to cover carbohydrate loading as an insulin during meals. It takes about 30 minutes for it to start working, but it might take anywhere from 10 to 75 minutes. The effect lasts for approximately eight hours, with a maximum duration of three hours (with a range of twenty minutes to seven hours). U-100 vials have a 31-day shelf life at room temperature. Regular (U-500) insulin is the same as human insulin, although it has different kinetics and is more concentrated than the U-100 formulation. Although the duration of action might last up to 24 hours, the onset is approximately 30 minutes [17].

**Intermediate Insulin and Long-Acting Insulin**

To reduce dosing errors, Glargine U-300 is exclusively available as a pen. When used at room temperature, it lasts for 42 days. The U.S. Food and Drug Administration (FDA) authorized the long-acting analogues insulin degludec U-100 and U-200 in September 2015. It is believed that the U-100 and U-200 are bioequivalent. Insulin degludec is modified by recombinant DNA in S. cerevisiae, and if a patient is allergic, they may react to the yeast. Insulin degludec works by forming soluble multi-hexamers, which allows for slow absorption and sustained activity [18].

**Table 5:** Does regimen [19]

| Regimen | Dose |
|---|---|
| Dosing according to weight | 0.7–1 units/kg per day in divided doses (no other advice is given). |
| Weight-based dosing plus trimester | TDD for the first trimester: 0.7 units/kg<br>TDD for the second trimester: 0.8 units/kg<br>TDD for the third trimester: 0.9–1 units/kg |
| | Given in the morning, two-thirds of TDD:<br>• 2/3 NPH with breakfast; 1/3 insulin as part or lispro<br>1/3 of TDD is administered at night:<br>• Half an NPH before bed; half an insulin as part or lispro with dinner |
| A one-dose-for-all approach | NPH: 20 units before bed and 20 units in the morning.<br>10 units of insulin as part or lispro should be taken at breakfast and dinner. |

**Insulin regimen**

If necessary, detemir insulin was always given prior to bed. NoVo Rapid insulin was usually administered prior to the main meals, if necessary. Not every patient required four daily insulin doses as part of a full basal-bolus protocol. Women were treated with one of the following regimens based on their glycaemic profile: quick acting insulin (1–3 times per day) if postprandial glycaemic levels were above targets; basal insulin alone if fasting glycemia was above targets; or a combination of basal and quick acting insulins if both fasting and postprandial levels were above targets [20].

**Metformin**

The "Metformin First" technique was used in a trial that showed increased patient acceptability, as seen by higher satisfaction ratings. Furthermore, metformin-treated pregnant women showed decreased rates of unfavorable outcomes, such as preterm delivery and the birth of large-for-gestational-age (LGA) babies. The main reason metformin works so well is that it may pass into the placenta thanks to organic cation transporters (OCTs), which are expressed there. In late pregnancy, Tertii *et al*. showed that 73% of the metformin was transferred from mother to fetus [21].

**Glyburide**

Glyburide, an oral hypoglycaemic medication, and insulin were once both advised for the treatment of GDM.5 Given that oral medications like glyburide are more cost-effective, easier to use, and more patient-accepted than insulin for the treatment of GDM, In the early 2000s, glyburide was used extensively in the US to treat GDM. Glyburide's safety and effectiveness in treating GDM, however, have come under scrutiny more recently. Glyburide was linked to a decreased chance of caesarean birth, but it was also linked to a higher risk of newborn hypoglycaemia and a longer length of stay in the intensive care unit, according to a recent meta-analysis of 24 studies comparing the perinatal effects of glyburide and insulin.8 [22].

**Glucose monitoring gdm**

Self-monitored blood glucose (SMBG) is the term for using a glucose meter to measure blood glucose at the fingertips of the hand. This is a practical and affordable method of comprehending real-time glucose values. The duration and magnitude of fluctuations are measured by continuous glucose monitoring (CGM) technologies, which measure dynamic glucose levels in daily life for 72 hours to 14 days, particularly during fasting and postprandial assessments. The use of CGM in GDM women is debatable, nevertheless. Numerous clinical studies have demonstrated that using CGM during pregnancy in GDM patients was linked to improved metabolic management and a lower risk of macrosomia in contrast to women who only use SMBG [23].

**Glycaemic Control Data**

Studies have indicated that between 80.6 and 91.2% of GDM cases have a HbA1c level less than 6%. GDM is defined as mild hyperglycemia in the second or third trimester. Therefore, prospective randomized clinical trials are required to precisely explain the CGM protocol during pregnancy and to determine the potential benefit of employing CGM in GDM women as opposed to solely SMBG in those with milder GDM (HbA1c <6%). The current study's objectives were to assess how CGM technology affected GDM in comparison to SMBG and to suggest logical advancements for glucose monitoring in patients with mild GDM [24].

**Closed-loop system**

Adults, adolescents, and children have all been the subjects of research on hybrid closed-loop (HCL) therapy.1–4 Both single and dual hormone administration automated insulin delivery devices are being studied.2–5 Pregnancies linked to diabetes have been researched using one experimental HCL system.6, 7 The first HCL system in the US, the Medtronic Mini Med 670G system (670G insulin pump, Guardian 3 Sensor for the continuous glucose monitor (CGM), and Contour Next Link blood glucose meter, manufactured by Medtronic in Northridge, California, was authorized by the Food and Drug Administration (FDA) in 2016.1, 8 It has two settings: auto and manual [25].

**Advanced Formulation Techniques for Gestational Diabetes Management:**

- **Microencapsulation**

**Microspheres:** Encapsulating insulin or oral hypoglycaemic agents in microspheres can improve bioavailability and reduce dosing frequency [26].

**Liposomes:** Liposomal formulations can enhance the delivery of insulin or oral hypoglycaemic agents, improving their efficacy and reducing side effects [27].

**Nanoparticles:** Nanoparticle-based formulations can improve the delivery of insulin or oral hypoglycaemic agents, enhancing their bioavailability and reducing dosing frequency [28].

- **Targeted Delivery Systems**

**Colon-Targeted Delivery:** Formulations designed to release insulin or oral hypoglycaemic agents in the colon can improve their bioavailability and reduce side effects [29].

**Liver-Targeted Delivery:** Formulations designed to target the liver can improve the delivery of insulin or oral hypoglycaemic agents, enhancing their efficacy and reducing side effects [30].

- **Controlled Release Systems**

**Matrix-Based Systems:** Matrix-based systems can provide controlled release of insulin or oral hypoglycaemic agents, improving their bioavailability and reducing dosing frequency.

**Reservoir:** Based Systems: Reservoir-based systems can provide a controlled release of insulin or oral hypoglycaemic agents, enhancing their efficacy and reducing side effects [31].

- **Nanotechnology-Based Formulations**

**Nanocrystals**: Nanocrystal-based formulations can improve the bioavailability and solubility of insulin or oral hypoglycaemic agents.

**Nanogels:** Nanogel-based formulations can provide a controlled release of insulin or oral hypoglycaemic agents, enhancing their efficacy and reducing side effects [32].

- **3D Printing-Based Formulations**

**Personalized Dosage Forms**: 3D printing can be used to create personalized dosage forms that meet the specific needs of individual patients.

**Complex Geometries:** 3D printing can be used to create complex geometries that provide controlled release of insulin or oral hypoglycaemic agents [33].

**Future Perspectives**

Because of industrialization and changes in lifestyle, the prevalence of diabetes is rising quickly. Research has focused on understanding the role of in utero circumstances and epigenetic mechanisms in the development of diabetes, in addition to hereditary and lifestyle variables. It highlights the necessity of developing fresh preventative strategies that prioritize the health of mothers and children. Compared to industrialized countries, diabetes is more common in underdeveloped countries. Diabetes is one of the largest health issues of the present and the future, and it is a major cause of medical care costs and mortality in the modern, globalized world. The prevalence of type 2 diabetes can be reduced by better living and economic circumstances. It provides a compelling argument in Favor of type 2 diabetes prevention and management initiatives [34].

**Conclusion**

Currently, Gestational Diabetes Mellitus (GDM) is primarily managed through lifestyle interventions, including dietary modifications, exercise, and blood glucose monitoring. When these are insufficient, insulin therapy remains the gold standard for treatment as it is safe and effective during pregnancy. Oral antidiabetic agents, such as metformin and glyburide, are also used in some cases, though their long-term safety for the fetus is still under investigation. In the future, advancements in precision medicine, AI-driven diagnostics, and continuous glucose monitoring systems will enable earlier detection and personalized treatment plans. Emerging therapies, including novel insulin analogs, incretin-based treatments, and gut microbiome modulation through probiotics, show great promise in improving glucose control with fewer

complications. Additionally, wearable devices, artificial pancreas systems, and telemedicine platforms will enhance patient monitoring and accessibility to care. In conclusion, while current treatments focus on lifestyle management and insulin therapy, the future of GDM care will emphasize personalized medicine, advanced technology, and innovative therapies, leading to better outcomes for both mothers and their children.

- Here is a table layout of marketed formulations for diabetes, including drugs commonly used in gestational diabetes:

| Drug class | Generic name | Brand names | Formulation | Uses |
|---|---|---|---|---|
| **Biguanides** | Metformin | Glucophage, glycomet, obimet | Tablet | First-line for gdm & t2dm |
| **Sulfonylureas** | Glibenclamide (glyburide) | Daonil, euglucon, semi-daonil | Tablet | Used off-label for gdm |
| **Insulin sensitizers** | Pioglitazone | Actos, pioz | Tablet | Not for gdm; for t2dm |
| **Dpp-4 inhibitors** | Sitagliptin | Januvia | Tablet | Used in type 2 diabetes |
| | Vildagliptin | Galvus | Tablet | Used in type 2 diabetes |
| **Sglt-2 inhibitors** | Dapagliflozin | Forxiga | Tablet | Not used in gdm; for t2dm |
| | Empagliflozin | Jardiance | Tablet | Not used in gdm; for t2dm |
| **Meglitinides** | Repaglinide | Prandin | Tablet | Used in type 2 diabetes |

1. Insulin (Ins) remains the first-line treatment for GDM.
2. Metformin (Met) is the most common oral alternative for GDM management.

Glibenclamide (Glyb) is used when insulin and metformin are unavailable or declined.

**Abbreviation table**

| Abbreviation | Full Form | Description |
|---|---|---|
| **GDM** | Gestational Diabetes Mellitus | High blood glucose during pregnancy. |
| **Met** | Metformin | Oral antihyperglycemic (Biguanide class). |
| **Glyb** | Glibenclamide (Glyburide) | Oral sulfonylurea, stimulates insulin release. |
| **Ins** | Insulin | Injectable hormone, gold standard for GDM. |
| **DPP-4** | Dipeptidyl Peptidase-4 Inhibitors | Oral drugs that increase insulin secretion. |
| **SGLT-2** | Sodium-Glucose Cotransporter-2 Inhibitors | Oral drugs that lower glucose via urine. |
| **T2DM** | Type-2 Diabetes Melitus | Chronic condition causing insulin resistance. |
| **BG** | Blood Glucose | Measurement to monitor glucose levels. |
| **HbA1c** | Haemoglobin A1c | Test for average blood glucose over 3 months. |
| **PPBG** | Postprandial Blood Glucose | Blood glucose after meals. |

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