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# **Beyond Pregnancy: Understanding the Long-Term Implications of Gestational Diabetes Mellitus**

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### ABSTRACT

The term "gestational diabetes mellitus," or GDM for short, refers to a hyperglycemic state that is initially identified during pregnancy, usually in the second or third trimester. At the moment, it is the most typical pregnancy-related medical issue. Around 15% of pregnancies worldwide roughly 18 million newborns annually—are affected by GDM. Preterm delivery and high birth weights are two fetal complications. Pre-eclampsia, postpartum abnormal glucose intolerance, and gestational hypertension are risks associated with GDM. Furthermore, GDM mellitus raises the possibility of problems like heart disease, obesity, and impaired glucose metabolism, culminating in type 2 diabetes in both the mother and the child. More focus and knowledge are needed about the rising incidence of GDM, which carries a substantial financial cost. It becomes imperative to have an in-depth comprehension of the pathophysiology and risk factors, with a focus on the impact of GDM in the emergence of non-communicable diseases. Additionally, an efficient treatment plan may be necessary to lessen perinatal and metabolic problems. Diet and physical activity are the main therapy for GDM. To step up the treatment, metformin, glibenclamide, and insulin can be employed. Based on the literature, this study offers a summary of the most recent findings about the etiology, diagnosis, therapy, and epidemiology of GDM. The significance of a diagnosis of GDM is emphasized as a potential indicator of non-communicable disease (NCD) risk in the future. Additionally, the impact of proper GDM management during and after pregnancy on the risk of NCDs in the mother and her kids is highlighted. An electronic search was conducted using Google Scholar, PubMed, and Scopus. Included were published research from 2014 to 2023 that described the epidemiology, diagnosis, risk factors, and treatment of GDM.

Keywords: Gestational diabetes, Maternal health, Fetal health, Hyperglycemia, non-communicable disease, Long-term outcomes

# INTRODUCTION

Diabetes mellitus is a metabolic condition with three distinct types viz:1, 2, and gestational; each with its own etiology, features, and treatment regimens. Diabetes mellitus is characterized by increased blood glucose levels due to insufficient or absent insulin [1-5]. Type 1 is more prevalent in children and is caused by the loss of  $\beta$ -cells and faulty insulin secretion; on the other hand, Type 2 is more common in adults and is caused by either inadequate insulin or resistance [6-9]. A 75-gram oral glucose tolerance test (OGTT) is conducted at 24-28 weeks' gestation to diagnose gestational diabetes mellitus (GDM), which is defined as a state of hyperglycemia with at least one of the following three values met: fasting plasma glucose level 92-125 mg/dL (5.1-7.0 mmol/L), 1hour plasma glucose level  $\geq 180 \text{ mg/dL}$  (10.0 mmol/L), and 2hour plasma glucose level ≥153 mg/dL (8.5 mmol/L). One of the most frequent medical issues during pregnancy is GDM, and if left untreated, it can have major negative implications on both the mother's and the child's health  $\lceil 10 \rceil$ . Based on the most recent statistics provided by the International Diabetes Federation, GDM affects about 14.0% of pregnancies globally, or about 20 million newborns yearly [11]. Women with GDM run a chance of experiencing pre-eclampsia, gestational hypertension, and cesarean delivery  $\lceil 12 \rceil$ . Additionally, GDM raises the risk of complications that can result in type 2 diabetes (T2DM) in both the mother and the child, such as obesity, cardiovascular disease, and altered glucose metabolism [13-15]. Greater focus and awareness are warranted due to the substantial economic burden associated with the rising incidence of GDM [16].

Despite extensive investigation, the etiology of GDM remains unclear; nevertheless, current understanding

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suggests a complex system combining several genetic, metabolic, and environmental variables [17]. A healthy diet combined with more exercise are the cornerstones of managing diabetes mellitus, including GDM. If these fail, pharmacotherapytypically insulin therapy-and oral hypoglycemic agents-primarily metformin and glibenclamideare also utilized [18-20]. In order to lessen the morbidity, complications, and financial effects of GDM on society, GDM must be prevented and

The incidence of diabetes, particularly GDM, is steadily rising among women of reproductive age, a trend largely attributed to the global plight of overweight and obesity [21]. The International Diabetes Federation (IDF) released a report in 2019

As one gets older, hyperglycemia during pregnancy becomes more common. This finding is supported by IDF data, which indicates that the age range of 45-49 has the highest percentage of pregnancies with GDM (37%). This age range was also associated with a reduced quantity of gestations with a correspondingly higher overall percentage of diabetes in this population  $\lceil 11 \rceil$ . Another significant factor that may raise the risk of GDM and DM2 by up to 20% is the delivery of a macrosomic child  $\lceil 22 \rceil$ . Pluriparity and the incidence of GDM continue to have a linear connection, even when the woman's age is taken into account [23]. The probability of recurrence is increased by more than six

If only risk groups are screened, as many as 35-47% of pregnant women may not receive a diagnosis of GDM, which will undoubtedly have an impact on the outcome of childbirth [27]. As a result, 75 g of glucose are now administered between weeks 24 and 28 of pregnancy to all pregnant women who have not previously been diagnosed with diabetes in order to establish the basis of GDM diagnoses. When a 75 g oral glucose tolerance test is performed, GDM is diagnosed during pregnancy if the fasting plasma glucose is  $\geq 5.1$ mmol/L, 1 h  $\ge$  10 mmol/L, and 2 h  $\ge$  8.5 mmol/L. The Australian Carbohydrate Intolerance Study in

Management of gestational diabetes

Because there aren't enough randomized clinical trials, it's very hard to provide a clear-cut care plan for GDM patients that will produce obstetric outcomes comparable to those of healthy women. Expert opinion and consensus are the foundations for the treatment of GDM. Cochrane Database Reviews analyses revealed a dearth of clear information about

# to how appropriate GDM management affects the risk of NCDs both during and after pregnancy.

# **Gestational diabetes Epidemiology**

that stated that more than 20.4 million women (14.0 percent of pregnancies) had problems with their metabolism of carbohydrates. Of these, about 80% had gestational diabetes (GDM), meaning that one in six babies was born with the condition  $\lceil 11 \rceil$ .

treated appropriately. This paper highlights the

significance of GDM as a potential future predictor of

non-communicable disease risk by summarizing

current studies on the genesis, diagnosis, treatment,

and epidemiology of the condition. It draws attention

# The Risk Factors for GDM

times if GDM was present in a prior pregnancy. The incidence of GDM is 12.3% in women with a BMI of at least  $30 \text{ kg/m}^2$ , and 11.6% in women with first-line relatives with a history of the disease. Up to 61% of instances of GDM are at increased risk when these two factors are combined [24]. Pregnant women who have polycystic ovarian syndrome are more likely to develop GDM. Research findings suggest that the occurrence of GDM is seasonal, with a higher incidence in the summer compared to the winter  $\lceil 25 \rceil$ . Furthermore, it was shown that pregnancies arising from in vitro fertilization had a 50% higher risk of GDM [26].

# Establishing a GDM diagnosis

Pregnant Women (ACHOIS) has shown that treating even minor forms of glucose intolerance in GDM provides an additional benefit. Research indicates that the incidence of obstetric problems is influenced by hyperglycemia and weight gain during pregnancy. Antihyperglycemic management was found to dramatically reduce newborn death, perinatal damage, hyperbilirubinemia, newborn hypoglycemia, and hyperinsulinemia in the ACHOIS trial. Additionally, there was a lower rate of weight increase [28].

# the relationship between obstetric outcomes and the degree of glycemic control [29]. According to Mitanchez et al. [30], a meta-analysis spanning the years 2014–2019 revealed that the most effective way to lower the incidence of obstetric problems is to combine food therapy with physical activity.

#### **GDM Dietary Therapy**

Numerous researches have established the beneficial impacts of dietary intervention in the treatment of a wide range of illnesses and in preserving a smooth pregnancy [31-35]. Adherence to nutritional guidelines aids in the achievement of normoglycemia, ideal weight gain, and appropriate fetal growth. The

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initiation of pharmaceutical treatment does not absolve the mother of her responsibility to adhere to the diet [36]. A customized diet plan is necessary for people with GDM. The mother's tastes, employment, relaxation, exercise, energy needs, macronutrient proportions, glycemic self-control, and BMI before to pregnancy should all be included in this approach [36]. According to Chao et al. [37], tailored advice for a particular GDM lady yielded better outcomes than generic ones. In order to prevent nocturnal hypoglycemia and morning ketosis, it is advised to have three main meals and two to three snacks each day, typically with a snack around 9:30 pm [38]. Using the diet and glycemic tool available online for 24 hours, a prospective observational trial showed that more frequent meals improved glycemic control [39]. Carbohydrates are the primary macronutrient in women with GDM, and consuming too many of them might result in hyperglycemia. However, glucose is essential to the placenta and fetus's healthy growth and metabolism since it serves as their primary energy substrate. As recommended by the American Dietetic Association, carbohydrate-rich foods with a low glycemic index should make up the majority of the diet's carbs, which should account for 40-50% of total energy required, or at least 180 g per day. A serving of roughly 600 g of fruit and

Although there are conflicting recommendations on exercise for women with gestational diabetes mellitus (GDM), observational studies do support safe physical activity throughout pregnancy. It's safe to engage in low-intensity fitness activities like walking, cycling, swimming, pilates, and badminton; it's safe to engage in strength training, badminton, tennis, and yoga. Contact activities, horseback riding, surfing, skiing, and diving should all be avoided by expectant mothers [44]. Aune et al. [45] have observed a 38% decrease in the threat of GDM in physically active ladies. According to an intervention trial conducted on overweight patients, women who exercised no more than three times a week had a 24% lower risk of developing GDM [46]. Based on an investigation by

Patients should receive pharmaceutical treatment if they are unable to meet their glycemic goals with a healthy meal and the eradication of food mistakes. The majority of research suggests that insulin therapy is the safest kind of care; oral medication should only be used if the patient refuses insulin therapy or it is not available [51]. It has been shown that using human insulin during pregnancy is safe [52]. Glibenclamide and metformin are now used orally. Despite crossing the placenta, metformin and glibenclamide are not anticipated to cause teratogenic effects [53]. Even though there is increasing evidence to support the use

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vegetables per day, with a minimum of 300 g of vegetables, whole grain bread, pasta, and rice, is the recommended daily intake of dietary fiber, which is 25-28 g [36]. Protein should make up roughly 30% of calories, or 1.3 g/kg of body weight/day, with 71 g of protein being the minimum daily recommended intake [36]. In the management of gestational diabetes mellitus (GDM), higher consumption of plant protein, lean meat and fish, and lower consumption of meats that are processed or red may enhance the response to insulin  $\lceil 40 \rceil$ . Due to possible hazards such placental malfunction, newborn obesity, inflammation, oxidative stress, and reduced maternal muscle glucose absorption, high fat diets-including those with less saturated fat—are not advised [40]. For the growth and development of the fetus, polyunsaturated fatty acids should be consumed during pregnancy instead of saturated fat. A twofold increased incidence of macrosomia is linked to weight gains above 18 kilograms [41]. Studies have shown that pregnant women should take 400 µg of folic acid, 5.0 µg of vitamin D, 500-900 mg of calcium, and 27-40 mg of iron daily as supplements. According to multiple research [42, 43], gut microbiota affects the development of GDM in the third trimester of pregnancy, but the benefits of probiotics in prevention or treatment are still unclear.

# Exercise as a GDM treatment

Ming et al. [47], increasing regular exercise in women with normal weight resulted in a 42% reduction in the incidence of GDM and a reduced weight gain during pregnancy without influencing the child's weight or the frequency of Caesarean sections. Women who engaged in 20–30 minutes of activity three–four times a week demonstrated a remarkable decrease in fasting and postprandial glucose levels, according to a metaanalysis of eight randomized trials conducted by Harrison et al. [48]. The United States PA recommendations, which found "strong" evidence of an inverse relationship between PA and the incidence of GDM, are similar to other evaluations' conclusions in this regard [49, 50].

# **GDM** Pharmacological Management

of metformin or glibenclamide for GDM, the American Diabetes Association and American College of Obstetricians and Gynecologists (ACOG) still recommend insulin as the first-line therapy if the glycaemic therapeutic objectives are not met with lifestyle changes. This recommendation stems from the lack of proof about the long-term safety of these alternative drugs [54]. It is not advised to utilize sodium-glucose cotransporter-2 (SGLT2) inhibitors while pregnant [53]. GLP-1 medicines have been used in GDM, according to certain research. GLP-1 drugs, such as glucagon-like peptide-1 receptor

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agonist (GLP-1 Ra) and dipeptidyl peptidase-4 (DPP-4) inhibitor, have been shown to improve insulin production in pancreatic b-cells and have numerous benefits in the treatment of type 2 diabetes  $\lceil 55 \rceil$ . However, GLP-1 treatments are not frequently prescribed for GDM. GLP-1 medications have been

Prevention of GDM: An avenue for lowering Type 2 DM and other non-communicable diseases Globally, non-communicable diseases (NCDs) are a major cause of maternal morbidity and mortality. Chronic diseases (NCDs) include a wide spectrum of illnesses that are of a chronic character, including diabetes, cancer, mental disorders, chronic respiratory diseases, and cardiovascular disease  $\lceil 57 \rceil$ . To reduce the burden of NCDs on affected women and their offspring, it is imperative to prevent and treat GDM both during and after pregnancy. When factoring out its transient, direct associations with adverse prenatal outcomes, antecedent GDM represents the strongest historical predictor of future Type 2 diabetes. Type 2 diabetes was almost 10 times more likely to strike women with GDM in later life  $\lceil 58 \rceil$ . Furthermore, there is a higher chance of cardiovascular disease in women with gestational diabetes [59]. There is an increased risk even in women who do not manifest overt Type 2 diabetes. Furthermore, when it comes to Type 2 diabetes in general, women with antecedent GDM seem to be at a higher risk than women without such a background [59]. Contrary to women with no GDM, women with the illness had a double higher chance of experiencing cardiovascular disease in the future. With postpartum

GDM presents a significant health concern globally, affecting approximately 14% of pregnancies worldwide. With the incidence of GDM on the rise, particularly among women of reproductive age, it is imperative to deepen our understanding of its pathophysiology, risk factors, diagnosis, and management. This manuscript underscores the multifaceted nature of GDM, highlighting its association with adverse maternal and fetal outcomes, including pre-eclampsia, gestational hypertension, and increased risk of type 2 diabetes for both the mother and child. Effective management strategies, encompassing dietary interventions, physical activity, and pharmacological treatments, play crucial roles in

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shown to regulate blood glucose, enhance insulin resistance, and lower the risk of postpartum diabetes in a review involving 516 patients. To prove their benefits, though, especially in pregnancy and in avoiding diabetes after birth, extensive clinical trials are required [56].

lifestyle modifications and possible medication use, it has been effectively established that there is a treatment opportunity to delay or prevent type 2 diabetes in women who are classified as "at risk" because of prior GDM [60]. Breastfeeding can be a highly helpful low-cost prophylactic intervention in preventing T2DM and associated metabolic derangements in women with a history of GDM, in addition to its other well-known benefits  $\lceil 61, 62 \rceil$ . Premature obesity in offspring raised in a hyperglycemic environment in utero increases the risk of type 2 diabetes, early impaired glucose tolerance, and long-term dangers of cardiovascular diseases. These dangers are not related to maternal obesity and are generally classified as "developmental origins of health and disease" [63]. GDM offspring are more likely to experience childhood problems, even when the mother's BMI is taken into account. The risk of offspring cardiovascular disease morbidity and childhood abdominal obesity are both increased by maternal gestational diabetes  $\lceil 64 \rceil$ . There may be a connection between GDM and neuropsychiatric problems in offspring, according to Nahum Sack and colleagues' research [65].

#### CONCLUSION

mitigating the risks associated with GDM and improving obstetric outcomes. Moreover, addressing GDM not only during pregnancy but also postpartum is crucial in reducing the long-term risk of type 2 diabetes and other non-communicable diseases for both mothers and their offspring. Prevention and management of GDM emerge as pivotal avenues in curbing the burden of non-communicable diseases and promoting maternal and child health on a global scale. Further research and concerted efforts are warranted to enhance prevention strategies, refine diagnostic approaches, and optimize therapeutic interventions for GDM to safeguard the health and well-being of future generations.

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