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DID YOU KNOW THAT GESTATIONAL DIABETES CAN ALSO OCCUR IN THE FIRST TRIMESTER OF PREGNANCY?

Dr. S. Gupta*
Dr. R.K. Gupta**
Dr. A. Agarwal***
Dr. M Sai Sushma Priya****
P. Gupta*****

Abstract

Background: *Gestational diabetes mellitus (GDM) is a form of diabetes that develops between 24-28 weeks of pregnancy and is characterized by elevated blood glucose levels that typically resolve after childbirth. According to recent research, it can also happen during the first trimester of pregnancy. The long-term implications of GDM also necessitate continuous monitoring of both mother and child to mitigate the risks of chronic diseases and to implement early interventions.*

Aim: *This review article intends to provide insights into the epidemiology of GDM, major contributing factors, screening and diagnostic criteria and complications. It also sheds light on the recent developments in the treatment guidelines for GDM, including the ADA and NICE guidelines.*

Method: *A screening of published articles has been conducted; followed by selection of relevant literature. Studies and guidelines pertaining to the various aspects of GDM have been studied and data from the same has been extracted for incorporating into this review paper.*

Results: *It has been found that the global prevalence of GDM has been rising, highlighting the need for timely diagnosis, addressing the risk factor and guideline-directed management. The increasing incidence can be attributed to several factors like genetics, obesity, maternal age and comorbidities as well. This has been discussed in detail in the presented review.*

Conclusion: *GDM is a growing public health concern due to obesity and lifestyle changes. It poses risks to both mothers and infants, including preeclampsia and increased risk of type 2 diabetes. Early diagnosis, management, and personalized treatment are hence crucial.*

Keywords: *Diabetes, GDM, ADA, NICE, Pregnancy.*

Introduction

Gestational diabetes mellitus (GDM) is a form of diabetes that develops during pregnancy and is characterized by elevated blood glucose levels that typically resolve after childbirth. GDM occurs in women without a prior diagnosis of diabetes but who exhibit hyperglycemia during pregnancy. The underlying mechanism often involves insulin resistance, exacerbated by the hormonal changes associated with pregnancy. As the pregnancy progresses, the body may struggle to produce sufficient insulin to maintain normal glucose levels, leading to elevated blood sugar levels.(1)

* MBBS, MS, Assistant Professor (Gynec & Obst Dept), SNMC, Agra, UP, India.
** M.B.B.S., M.D, FIACM, FISC, FIAE, FIDA, Assistant Professor FH medical college, Agra, India.
*** MD, DM, FESC, Ex Assistant Professor Cardiology, J.L.N. Medica College, Ajmer, Rajasthan, India.
**** Pharm.D, Junior Researcher, Agra Medicity Hospital, Agra, India.
***** MBBS, Student Government Autonomous Medical college, Firozabad, UP, India.

The impact of GDM extends beyond immediate maternal health concerns, affecting both the mother and the developing fetus. Maternal health implications include an increased risk of chronic conditions, such as type 2 diabetes, cardiovascular disease, and chronic kidney disease, as well as pregnancy complications like gestational hypertension and the need for cesarean delivery.(2) For the fetus, the risks include macrosomia, metabolic disorders, and immediate neonatal complications like hypoglycemia, respiratory distress syndrome, and jaundice. The long-term implications of GDM also necessitate continuous monitoring of both mother and child to mitigate the risks of chronic diseases and to implement early intervention strategies.(3)(4)

Prevalence and Incidence

Gestational diabetes mellitus (GDM) is increasingly recognized as a significant public health issue, with its prevalence and incidence reflecting broader trends in maternal health, lifestyle changes, and obesity rates. Globally, the prevalence of GDM is estimated to be around 14%, with variations depending on the population studied and the diagnostic criteria used. Regional differences in prevalence are significant, influenced by genetics, lifestyle factors, and healthcare access.(5) For example, in North America, the prevalence ranges from 7% to 9%, with higher rates observed in specific populations, such as Hispanic and African American women.(6) In Asia, particularly India, a systematic review found a pooled prevalence of 16.1%, with notable regional discrepancies, and some states reporting rates as high as 17.8%. In the Middle East, the prevalence can exceed 25%, reflecting prevalent lifestyle factors and genetic predispositions.(7,8)

The incidence of GDM has been rising globally, largely due to increasing obesity rates and lifestyle changes. The global obesity epidemic, particularly among women of childbearing age, is a significant risk factor for GDM, with higher rates observed in populations with elevated obesity prevalence. Sedentary lifestyles and unhealthy dietary patterns also contribute to the increasing incidence of GDM. Moreover, improved screening practices and enhanced awareness have led to higher reported prevalence rates, reflecting both a true increase in incidence and better detection. Longitudinal studies indicate that the prevalence of GDM is increasing by approximately 7% per year in certain populations, underscoring the urgency of addressing this growing public health concern(6,9,10)

Timing of Occurrence

Gestational diabetes mellitus (GDM) is typically diagnosed between 24 and 28 weeks of gestation. This timing is crucial as it aligns with the physiological changes that occur during pregnancy, which influence glucose metabolism. The standard practice for diagnosing GDM involves universal screening during this period.(11,12) The American College of Obstetricians and Gynecologists (ACOG) recommends a two-step screening approach: an initial one-hour glucose challenge test (GCT) using a 50g oral glucose solution, followed by a confirmatory 100g three-hour oral glucose tolerance test (OGTT) if the results are abnormal(13).

Contributing Factors

- **Impact of BMI on GDM Development**

Obesity and overweight are important risk factors for GDM, with a greater pre-pregnancy BMI substantially raising the chance of getting the illness. Obese women have a four-fold increased risk of GDM compared to normal weight women, and maternal obesity is a risk factor for type 2 diabetes, hypertension, and cardiovascular disease (14). Because of its localized inflammation and altered adipokine expression, adipose tissue may be important in the etiopathogenesis of GDM. Obese women also exhibit systemic insulin resistance, with increased inflammatory markers in their bodies leading to a higher risk of developing GDM (15). Women of Chinese and South Asian descent have a markedly increased risk of developing GDM, and lower BMI cut-offs for Asian populations may need to be considered in GDM prevention initiatives (16). Research has connected being overweight or obese to the clustering of metabolic risk factors in the early stages of pregnancy and the chance of developing GDM. Interventions targeting reducing pre-pregnancy weight can significantly reduce the risk of developing GDM (17–19).

- **Central obesity as a Risk Factor**

Central obesity, characterized by excessive abdominal fat accumulation, is a significant risk factor for GDM (20). This is due to the accumulation of visceral fat, which produces inflammatory cytokines, leading to impaired glucose regulation and insulin resistance (21). A recent meta-analysis found a correlation between viscera adipose tissue depth and GDM (22). A Chinese study found that

larger waist-to-hip and waist-to-height ratios during the first trimester of pregnancy are linked to a higher risk of GDM (23). GDM risk can be decreased by preventing the accumulation of abdominal fat before and during pregnancy, and women who are centrally obese should get further counseling (24).

- **Family History and Genetic Predisposition of Diabetes: Risk Factors for GDM Development**

Genetic predisposition is a major contributing element to the development of GDM, with family history playing a substantial influence. Having a family history of diabetes, mainly type 2 diabetes, is strongly associated with an increased risk for GDM. Multiple genetic loci identified as having relations with T2DM could also have a bearing on susceptibility to GDM (25). Variants at the TCF7L2, PPARG, and GCK genes have been implicated in glucose metabolism and insulin resistance, key characteristics in the development of GDM. Variants at the TCF7L2 gene may lead to a decrease in β-cell function and a reduction in insulin sensitivity, thus increasing the risk for GDM (26,27). Polymorphisms in PPARG have been linked to an enhanced risk of developing Type 2 diabetes and GDM, indicating that this gene also plays a minor role in metabolic procedures involved in GDM risk. The GCK gene encoding glucokinase has also been associated with diabetes risk (28).

- **Risk of GDM Recurrence**

A history of GDM is a significant risk factor for its recurrence in future pregnancies. This risk depends on the severity of the first episode and pre-pregnancy weight, as well as other factors (29). The history of GDM may indicate a defect in beta-cell function, which can persist between pregnancies and increase the risk of recurrence (30). Additionally, those with a history of GDM are more likely to develop cardiovascular disease in the future. A study in China found a significant association between GDM recurrence and age, high BMI, macrosomia, OGTT level, impaired fasting glucose, and abnormal OGTT results (31,32).

- **Ethnic Variations**

GDM incidence varies significantly based on ethnicity. Women from South and Southeast Asia, particularly those from India, Pakistan, and Bangladesh, have a higher risk of developing GDM due to higher insulin resistance and body fat distribution (33,34). Hispanic women also have a higher risk due to genetic predisposition, obesity, and lower physical activity. African American women are also at higher risk due to higher pre-pregnancy obesity rates (35). A study by Hedderson *et al.* found that non-Hispanic white women had the lowest rates of GDM, while Asian Indian women had the highest rates. Foreign-born Korean and Japanese women were less likely to develop GDM. GDM occurs in 3% to 7% of pregnant women in the US, with Asian, black, American Indian, and Hispanic women at an increased risk (36). It is crucial to create a diabetes screening and preventive program that works for women with GDM, especially for black women with the disease (37).

- **The Influence of Maternal Age**

Maternal age is a major risk factor for GDM, with older women particularly those over 35, having a larger chance of getting the illness while pregnant. This is due to physiological and metabolic changes associated with aging, such as insulin resistance, obesity, and changes in glucose metabolism and endocrine regulation (38). Studies have shown that GDM is linked to increased risks of preterm birth, macrosomia, LGA, and cesarean delivery in Chinese urban women (39). Women with chronic conditions may be more vulnerable during pregnancy, necessitating increased monitoring and surveillance. Advanced maternal age is associated with an increased likelihood of other comorbid states, such as hypertension and dyslipidemia, which increase the risk of GDM (40). Thus, in order to reduce the risk of GDM and guarantee the best possible outcomes for moms and their children, early screening and proactive management strategies are essential. (41).

- **Polycystic ovary syndrome (PCOS) and Hypertension as Risk Factors**

Hypertension and PCOS are significant risk factors for GDM. PCOS is characterized by metabolic dysfunction and insulin resistance, which are linked to polycystic ovaries, hyperandrogenism, and irregular menstrual cycles (42). Women with PCOS are more likely to have higher levels of insulin resistance and reduced glucose tolerance, making them at risk for GDM (30). Obesity and increased maternal age are linked to a higher risk of GDM in PCOS-afflicted women. PCOS is also an independent risk factor for preeclampsia and gestational weight gain, necessitating close monitoring of blood pressure, blood glucose, and body weight. Pre-existing or early pregnancy-onset hypertension increases

the risk of GDM, and screening for GDM in women with hypertension is warranted. Effective prenatal and intrapartum therapy may reduce the risk of GDM and improve overall health outcomes (45).

Screening, Diagnostic Tests & Criteria for GDM

- **Screening: Universal screening**

The global prevalence of GDM is increasing, particularly in Asian populations like India. The likelihood of acquiring diabetes later in life is increased by GDM, as are consequences for both mothers and fetuses. Factors like infertility, advanced maternal age, obesity, family history, and parity are strongly linked to GDM. Universal screening for GDM should be compulsory in high-prevalence areas like India (46). Early universal screening detects more cases of GDM, most before 20 weeks of gestation. This screening strategy could be adapted for high-risk or high-prevalence settings (47).

- **Diagnostic Tests**

GDM is diagnosed using either a two-step or one-step approach. The two-step method involves a 50-gram oral glucose challenge test (OGCT) taken between weeks 24 and 28 of pregnancy without fasting. An oral glucose tolerance test is given if the results meet or above the screening criteria. The one-step approach provides a 75-gram glucose load after measuring plasma glucose levels at one and two hours after fasting. The fasting plasma glucose test (FPG) is a diagnostic tool for GDM, measuring blood sugar levels after an overnight fast. Raised FPG can be an excellent predictor, especially in women with other risk factors or symptoms. Regular monitoring and doctor follow-up are crucial for managing complications associated with GDM (48).

- **Diagnostic Criteria**

The American Diabetes Association advises glucose testing for GDM from 24 to 28 weeks of gestation in all asymptomatic pregnant women. One-step screening can be performed using the IADPSG criteria, while two-step screening can be performed using the Carpenter and Coustan criteria. Diagnosis criteria for GDM include fasting glucose levels 5.1 mmol/l, 1 hour 10.0 mmol/l, and 2 hour 8.5 mmol/l. Critics argue these criteria exaggerate the diagnosis and may result in unnecessary interventions. Every 1-3 years, those with a history of GDM should undergo lifetime screening to check for the onset of type 2 diabetes or prediabetes, as per the ADA 2024 recommendations (49).

Treatment Guidelines

- **ADA Guidelines**

Under the ADA 2023 guidelines, the management of gestational diabetes mellitus (GDM) involves a comprehensive approach encompassing lifestyle modifications, pharmacotherapy, and regular monitoring. The primary goals are to achieve and maintain optimal glycemic control to minimize both maternal and neonatal complications.

Lifestyle Modifications

The cornerstone of GDM management is lifestyle modification, which includes dietary adjustments and increased physical activity. The ADA recommends a personalized dietary plan designed to meet caloric and nutritional needs while maintaining appropriate blood glucose levels. Patients are encouraged to engage in moderate-intensity physical activity, such as walking, or other types of effective exercise (aerobic, resistance, or both) for 20–50 min/day, 2–7 days/week. These interventions are often effective in managing blood glucose levels and can delay or prevent the need for pharmacological treatment in many cases(4,50). Glucose monitoring aiming for the goals recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus are:

- Fasting glucose <95 mg/dL (<5.3 mmol/L) and either
- One-hour postprandial glucose <140mg/dL (<7.8 mmol/L) or
- Two-hour postprandial glucose <120mg/dL (<6.7 mmol/L)

Medical Nutrition Therapy

The recommended dietary intake for pregnant individuals includes at least 175 grams of carbohydrates (35% of a 2,000-calorie diet), a minimum of 71 grams of protein, and 28 grams of fibre. The nutrition plan should prioritize monounsaturated and polyunsaturated fats while minimizing saturated fats and avoiding trans fats. As with all dietary management for diabetes, the type and amount of carbohydrates consumed directly affect glucose levels. Emphasizing high-quality, nutrient-dense carbohydrates can lead to better control of fasting and postprandial glucose levels, reduced free fatty

acids, improved insulin sensitivity, and vascular benefits, potentially decreasing excessive infant weight gain. Conversely, replacing carbohydrates with fats may inadvertently increase lipolysis, elevate free fatty acids, and exacerbate maternal insulin resistance.(51)

Pharmacotherapy

When lifestyle modifications are insufficient to achieve glycemic targets, pharmacotherapy may be necessary. Insulin therapy is considered the first-line medication for managing GDM. Insulin has a long history of use and is effective in controlling blood glucose levels without crossing the placenta(52).

Oral hypoglycaemic agents, particularly metformin and glyburide, are alternative options for patients who cannot use insulin or prefer not to. Metformin, a biguanide, is used to improve insulin sensitivity and lower blood glucose levels. Glyburide, a sulfonylurea, stimulates insulin secretion from the pancreas. Both agents have been shown to be effective and safe for many patients with GDM, although ongoing monitoring is required to ensure they do not adversely affect the mother or foetus. Metformin and glyburide, individually or in combination, should not be used as first-line agents, as both cross the placenta to the foetus.(53)

- **National Institute for Health and Care Excellence (NICE) Guidelines**

The National Institute for Health and Care Excellence (NICE) provides comprehensive guidelines for the management of gestational diabetes mellitus (GDM), focusing on early detection, effective treatment, and ongoing monitoring to improve outcomes for both mother and baby.

  - **Initial Management**

NICE recommends that all pregnant individuals be offered screening for GDM at 24-28 weeks of gestation using a 75-gram oral glucose tolerance test (OGTT) if they are at risk. For those with risk factors such as obesity or a history of GDM, earlier screening may be advised [4]. Upon diagnosis, the primary goal is to achieve optimal glycemic control through a combination of lifestyle changes and, if necessary, pharmacological treatment.

  - **Lifestyle Modifications**

NICE guidelines emphasize the importance of lifestyle modifications as the first-line treatment for managing GDM. Patients should receive guidance on a balanced diet, focusing on low-glycemic index foods, and be encouraged to engage in regular physical activity. Dietary advice should aim to regulate blood glucose levels while ensuring adequate nutrition(54)

  - **Pharmacotherapy**

If lifestyle modifications alone do not achieve adequate glycemic control, NICE recommends considering pharmacotherapy. Insulin is the preferred medication for managing GDM when oral agents are not effective or suitable. NICE acknowledges the role of oral hypoglycaemic agents, specifically metformin and glyburide, for patients who are unable to use insulin or prefer oral medications. Metformin improves insulin sensitivity, while glyburide stimulates insulin secretion.

  - **Monitoring and Follow-Up**

Regular monitoring of blood glucose levels is essential to assess the effectiveness of the treatment regimen. NICE advises regular self-monitoring of blood glucose and periodic follow-ups with healthcare providers to adjust treatment as needed. Postpartum care includes screening for type 2 diabetes 6-12 weeks after delivery and providing ongoing follow-up to monitor long-term health.

  - **Special Considerations**

NICE guidelines also include recommendations for managing GDM in special situations, such as in the presence of multiple pregnancies or significant fetal growth abnormalities. In these cases, additional monitoring and more intensive management may be necessary.(54)

Complications and Outcomes

- **Maternal Complications**

Gestational diabetes mellitus (GDM) significantly impacts maternal health, increasing the risk of several complications. Key issues include:

  - **Preeclampsia:** Women with GDM face a higher risk of developing preeclampsia, which can lead to severe health problems for both mother and child (American Diabetes Association, 2023).

- **Increased Likelihood of Caesarean Delivery:** GDM often results in macrosomia (excessive fetal growth), which may necessitate caesarean delivery to avoid complications during birth (International Diabetes Federation, 2023).(55)
- **Postpartum Diabetes Risk:** Women with GDM are at an elevated risk of developing type 2 diabetes later in life, necessitating ongoing monitoring and lifestyle modifications (Society for Maternal-Fetal Medicine, 2024).(56)

- **Fetal Complications**

  The fetus is also at risk of various adverse outcomes when the mother has GDM, including:

  - **Macrosomia:** Elevated blood glucose levels can lead to excessive fetal growth, increasing the likelihood of delivery complications and long-term health issues for the child (American Diabetes Association, 2023).
  - **Neonatal Hypoglycemia:** Newborns may experience low blood sugar levels, which can cause immediate health concerns and require careful management immediately after birth (International Diabetes Federation, 2023).(55)
  - **Preterm Birth:** GDM can increase the risk of preterm birth, which can impact neonatal health and development (Society for Maternal-Fetal Medicine, 2024).(56)

Postpartum Care

Effective postpartum care for individuals with Gestational Diabetes Mellitus (GDM) is essential due to the increased risk of persistent glucose intolerance or progression to type 2 diabetes. This review outlines the critical aspects of postpartum management, incorporating the latest guidelines and evidence-based practices:

- **Postpartum Diabetes Screening and Monitoring**
  - **Initial Testing:** Women with a history of GDM should undergo testing for persistent diabetes or prediabetes at 4–12 weeks postpartum using a fasting 75-g oral glucose tolerance test (OGTT). The OGTT is preferred over HbA1c due to its greater sensitivity in detecting glucose intolerance following pregnancy-related changes. If the OGTT reveals any abnormal values, a repeat test is necessary for confirmation.
  - **Ongoing Surveillance:** Continuous monitoring for prediabetes or type 2 diabetes is recommended every 1–3 years, regardless of initial postpartum test results. This may involve annual HbA1c, fasting plasma glucose tests, or triennial OGTTs.(57)
- **Risk Assessment and Lifestyle Interventions**
  - **Long-term Diabetes Risk:** Women with GDM face a significantly elevated lifetime risk of type 2 diabetes, with an estimated 50–60% likelihood of developing the condition over time. The risk increases progressively, reaching 60% by age 50.(57)
  - **Lifestyle Modifications:** Adopting healthy eating patterns and managing weight effectively postpartum can substantially lower the risk of developing type 2 diabetes. Evidence shows that weight management and lifestyle interventions can mitigate the risk, with lifestyle changes reducing diabetes progression by 35% and metformin by 40% over 10 years (American Diabetes Association, 2023; National Institutes of Health, 2024).
- **Weight Management and Preventive Strategies**
  - **Weight Management:** Postpartum weight management is crucial, as interpregnancy weight gain and higher BMI are associated with increased GDM risk and subsequent type 2 diabetes. Effective weight loss strategies are recommended for those with BMI >25 kg/m² to reduce future risk.
  - **Preventive Interventions:** Lifestyle interventions and medications like metformin are effective in preventing or delaying diabetes onset. Ensuring that these interventions continue postpartum can help maintain health gains achieved during pregnancy (American Diabetes Association, 2023; National Institutes of Health, 2024).

Preventive Measures

Diabetes during pregnancy increases the risk of complications for both the mother and her baby, which can be costly for individuals and society. Preconception counseling can help prevent these costs by improving knowledge, attitudes, and behaviors about preconception health, modifying risks of adverse

pregnancy outcomes, and reducing health disparities (58). Preconception care (PCC), a continuum of care, emphasizes good glycemic control, a healthy diet, medication adjustments, baseline laboratory values, and retinal exams. The significance of attaining glucose levels as near to normal as is reasonably feasible, ideally, an A1C <6.5% should be covered in preconception counselling to lower the risk of congenital defects, preeclampsia, macrosomia, premature birth, and other problems (59).

Gestational diabetes mellitus (GDM) is a growing public health concern, linked to rising obesity and lifestyle changes. It poses significant risks to both mothers and infants, including preeclampsia, macrosomia, and an increased likelihood of developing type 2 diabetes. Early diagnosis through screening, particularly the Oral Glucose Tolerance Test (OGTT), and effective management with lifestyle changes and pharmacotherapy are crucial. The integration of continuous glucose monitoring is enhancing GDM care, while personalized treatment approaches are becoming more prevalent. Postpartum follow-up is essential due to the high risk of type 2 diabetes in women with a history of GDM. Public health interventions, especially in low- and middle-income countries, are vital for prevention and management. Addressing GDM requires a comprehensive approach that includes early detection, personalized care, and ongoing support to mitigate long-term health risks for both mothers and children.

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