GESTATIONAL DIABETES MELLITUS – FROM RISK FACTORS TO PREVENTION

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DOI: https://doi.org/10.71419/mtggrc.2025.30

ABSTRACT

Gestational diabetes mellitus (GDM) is the most common pregnancy complication globally. GDM prevalence ranges from <3% to >20%. One in 5 livebirths is affected by hyperglycemia in pregnancy (HIP), and 1 in 6 is explicitly affected by GDM. HIP is classified as pregestational diabetes, gestational diabetes, and diabetes in pregnancy. 75%-90% of HIP cases are GDM.

Diverse environmental, socioeconomic, and individual risks play a pivotal role in the global rise in GDM. *Environmental risks* affect the gut microbiome, causing oxidative stress, inflammation, insulin resistance, neurohormonal/β-cell dysfunction, and genetic/epigenetic modification. These factors are associated with an increased risk of GDM and its short-term/long-term complications. A "neglected pollutant" (artificial light/noise) causes significant damage to women's health. Light pollution (screen light, streetlights, artificial light at night) causes circadian rhythm and sleep disorders that lead to GDM. Mothers with *low socio-economic status* (an index assessing educational level and employment) have an increased risk of GDM. There is a wide range of *individual risks* – reversible (obesity, passive lifestyle, unhealthy diet, smoking, stress, etc) and irreversible (maternal age, family history of DM/GDM, miscarriages/stillbirth in previous pregnancies, etc). The more risk factors a woman has, the higher her risk of GDM. Undiagnosed/untreated GDM is associated with a wide range of maternal complications during pregnancy, labor, postpartum, and beyond, and fetal congenital/neonatal complications. Though GDM is not preventable, its risk can be lowered – the ideal time to influence GDM risks is around pregnancy. Elimination of reversible risks is essential to halt the global rise of GDM. Its screening, treatment, and management reduce feto-maternal morbidity/mortality.

Keywords: gestational diabetes mellitus; environmental and socio-economic risk factors; individual risk factors; feto-maternal outcomes; screening, prevention

Introduction

According to the UNO and WHO, four basic non-communicable diseases (NCDs) are: cardiovascular diseases (CVD), diabetes mellitus (DM), including gestational diabetes (GDM), cancer, and chronic respiratory diseases. All NCDs are programmed and imprinted during pregnancy. Thus, hyperglycemia during pregnancy can change fetal programming with metabolic complications in adult life! GDM is one of the three main types of DM, it is one of the most common complications during pregnancy globally. One in 5 live births is affected by hyperglycemia in pregnancy, and 1 in 6 is explicitly affected by GDM. Its prevalence varies from less than 3% (Norway/2% and Sweedent/2.5%) to more than 20% (Spain/37.6%, Malasya/27.3%, Thailand/26.5%, Germany/26.1%, India/26.1%, UK/23.1%, South Korea/21%, Vietnam/21%).[1,4]

Classification

According to the WHO and the International Federation of Gynaecology and Obstetrics (FIGO)/ International Diabetes Federation (IDF) Joint Statement (2018), hyperglycaemia in pregnancy (HIP) can be classified as pregestational diabetes, gestational diabetes (GDM), or diabetes in pregnancy (DIP).[2,3]
Pre-gestational diabetes is type 1, type 2, or other rarer forms of diabetes that were diagnosed in pregnant women before conception. DIP is hyperglycaemia first diagnosed during pregnancy, meeting the WHO criteria of diabetes in non-pregnant women.[4]
Available data indicate that 75% to 90% of HIP cases are GDM, which occurs in 2-10% of all pregnancies (Tables 1 and 2).[4]

Table 1. Global estimates of hyperglycemia in pregnancy in 2024 (total live births to women aged 20-49 years in millions)

Hyperglycemia in pregnancy	
Global prevalence	19.7%
Number of live births affected in millions	23.3 million
Proportion of cases due to GDM	79.2%
Proportion of cases due to odiabetes (T1/T2) first detected in pregnancy	9.9%
Proportion of cases due to diabetes detected prior to pregnancy	11%

Table 2. Hyperglycemia in pregnancy in the European region in 2024 (total live births to women aged 20-49 years in millions)

Age-adjusted prevalence (%)	Raw prevalence (%)	Number of live births affected in millions
14.2	15.9	1.5

GDM may occur at any time during pregnancy and, generally, disappears after the baby is born. However, the risk of developing T2DM in future life or GDM in subsequent pregnancies remains very high.

What Is GDM?

The World Health Organization (WHO) defines GDM as “any level of the early or first detection of glucose intolerance in pregnancy”. Gestational diabetes mellitus (GDM) is a non-communicable disease affecting pregnant women. It is a condition in which human placental lactogen (HPL) prevents the body from using insulin effectively. It leads to hyperglycemia and gestational diabetes. GDM is a condition in which a woman without diabetes develops high blood sugar levels, which is first diagnosed during pregnancy and generally resolves at birth.

There are two types of GDM, which are categorized based on the treatment required to keep blood sugar levels in an optimum range:

- A1GDM - known as "diet-controlled gestational diabetes" (it can be managed without medication), and
- A2GDM - this type needs to be treated with medicine.[5]

Although the cause of GDM is not known, there are some theories as to why the condition occurs. And risk factors, without doubt, play an important role.

What Are the Risk Factors Associated with GDM?

The environmental, socioeconomic, and individual risk factors associated with GDM play a pivotal role, causing a constant global rise in GDM prevalence over the past two decades.[6]

GDM and Environmental Risk Factors

Experimental studies suggested that the potential biological mechanisms of environmental pollutants**,** such as ratio of grey space-to-green space, buildings and city planning,walkingand recreation spaces; food environment; soil and water pollution, air pollution with, such polutants as oxinitrides - NOX, NO, NO_2; CO, SO_2, O_3; climate factors, such as seasons or very high ambient temperature in spring and summer and hot weather; chemicals and metals (methyl mercury, cadmium, tributilene, arsenic, phthalates, phenols, titanium dioxide/TiO_2, mercury/methylmercury) in sea food; persistent organic pollutants (pesticides, industrial chemicals, etc) all affect gut microbiom, cause oxidative stress, inflamation, insulin resistance, neurohormonal and β-cell dysfunction, and epigenetic modification. All this might be associated with an increased risk of GDM and its short-term and long-term complications.[7]

Bisphenol A (BPA) is an endocrine-disruptor that is used in the production of polycarbonate plastics. There is evidence that maternal exposure to BPA, even among pregnant women of normal weight, is associated with an increased risk of GDM. BPA, and its analogues BPS, BPF, and BPAF, are detected in indoor dust samples and food and beverages, which indicates a constant harmful exposure to bisphenols.[8-12]

Other "neglected pollutants" that cause significant damage to human health are light (artificial) and noise. High levels of road traffic noise adversely affect 40% of the population. Light pollution (including the use of phones, computers, tablets, and watching TV before going to bed, as well as street lights) may be associated with the increased risk of GDM. A study demonstrates that it causes circadian rhythm and sleep disorders that can disrupt glucose metabolism.[13]

GDM and Socio-Economic Risk Factors

According to results from the Generation R Study, low maternal educational level promoted the development of GDM.[14-15]

An Italian study from Turin found that mothers with low socioeconomic position (a composite index assessing educational level and employment) were at a higher risk of developing GDM.[16]

GDM and Individual Risk Factors

The leading individual risk factors of GDM are:

- Age ≥35 years, or decreased function of internal organs (in particular, the pancreas)
- High BMI prior pregnancy: overweight (>25 kg/m²) and obesity(>30 kg/m²);
- Gaining too much weight (>10kg) in the 1-st trimester of the current pregnancy;
- Family history of type 2 DM and GDM (in the 1-st-degree relatives);
- Pre-diabetes;

- History of GDM, previous infant with birth weighing >4000 g, previous stillbirth and/or recurrent abortions (>3 in previous pregnancies), fetal malformations, preterm delivery (<37 gestational weeks), Cesarean section, multiple pregnancy (2-3 fetuses);
- HbA1c >5.7;
- Glucosuria in the current pregnancy;
- Abnormal OGTT (oral glucose tolerance tests);
- Dyslipidemia (low HDL-CH,TR >200 mg/dl);
- Hypertension (chronic and pregnancy-induced);
- Conditions associated with insulin resistance - Polycystic Ovary Syndrome (PCOS) and Acanthosis Nigricans;
- Polihydramnio.

Such individual, habitual risk factors as low physical activity, glucocorticoid administration, and smoking play an important role in the development of all non-communicable diseases, including GDM![17,18]

Stress of any form has the potential to exacerbate GDM risk independently.[19]

Smoking specifically causes insulin resistance, leading to obesity and pre-diabetes, thus aggravating the risk of GDM. It carries triple dan for a:

- woman, especially a pregnant one;
- fetus, and
- future generations.[20]

The more risk factors a woman has, the higher the risk of developing GDM. In the presence of multiple risk factors, supervision by a multidisciplinary team is required.

It is preferable if supervision is initiated well before conception.

Hyperglycemia in Pregnancy and Maternal Age

Risk of hyperglycemia during pregnancy increases with maternal age, reaching its peak at the age of 45-49 years (42.3%). Since the majority of pregnancies and births occur at <30 years of age (46.3%, or 9.8 million), the majority of cases of hyperglycemia in pregnancy occur in this age group.

One of the meta-analyses, published in 2020, demonstrates that the risk of GDM increases linearly with successive age groups.[21]

However, over the last few decades, there has been an increase in the number of primigravida aged 35 years and older.

Risks Categories of GDM

Risk of GDM development falls into the following three categories:

High Risk:

- Pre-diabetes
- History of GDM
- Long-term (more than three courses/year) steroid use at a daily dose of ≥5mg
- Pre-existing CVD
- Ethnicity
- Obesity (BMI ≥30 kg/m^2)
- Waist circumference >80cm females

Moderate Risk:

- Physical inactivity
- Energy-dense Western-style diet
- Smoking

- Family history of DM
- Hypertension
- PCOS
- Metabolically-dysfunction-associated steatotic liver disease (MASLD)
- Low socioeconomic status
- Age >45 years

Low Risk:

- Age <45 years, with absence of any of the above

GDM and Conditions That Increase the Risk of fGDM

Duration and Quality of Sleep

Evidence demonstrates that sleep disorders may increase pregnancy complications, including GDM. Obstructive sleep apnea (OSA) is the most common form of sleep-disordered breathing. It was shown that OAS increases the risk of GDM. Short and long sleep durations have also been linked to GDM. An association between poor sleep quality and GDM has been observed; however, it remains unclear whether improved sleep duration and/or quality will lead to improved glucose metabolism.[22-24]

Vitamin D Deficiency

Vitamin D deficiency has been increasingly recognized as one of the potential contributors to GDM development. A recent meta-analysis has shown that vitamin D deficiency is associated with the risk of GDM. The relation between GDM and vitamin D deficiency seems to be a two-way street, as

- Low values of vitamin D increase the risk of GDM;
- Women with GDM were more likely to develop vitamin D deficiency compared to pregnant women with normal vitamin D levels.

Unfortunately, no large randomized controlled trial on vitamin D in women at high risk for GDM has been published as yet, and it remains to be proved whether vitamin D deficiency contributes to the development of GDM.[25-28]

Thus, any clinical conclusions should be interpreted with caution.

GDM and Metabolically Associated Steatotic Liver Disease (MASLD)

MASLD may be a risk factor for the development of any type of DM, including T1, T2, or GDM. There is a bilateral positive association between MASLD and GDM:

- Studies reported that MASLDrisk is significantly higher in women with GDM. GDM is a new risk factor for MASLD that affects the course of the disease independently throughout life.
- Still other studies reported that the GDM development risk was substantially higher in women who, independent of their BMI (normal or elevated), were diagnosed with MASLD. GDM is associated with increased postpartum risk for MASLD[29,30]

Feto-Maternal Complications of GDM

GDM is associated with a wide range of both maternal complications during pregnancy, labor, postpartum, and beyond, and fetal congenital and neonatal complications and poor long-term outcomes.[31]

Feto-Maternal Outcomes of GDM and the Role of GDM Screening

GDM is a major pregnancy complication associated with increased morbidity and mortality for the mother, fetus, and baby. A fetal and neonatal mortality rate was as high as 65% before

the development of specialized maternal and neonatal care.GDM that stays undiagnosed and untreated results in adverse pregnancy outcomes.

Thus, the purpose of screening, treatment, and management of GDM is aimed at the prevention of poor pregnancy outcomes.

GDM screening is important, as it:

1. reduces maternal, fetal, and newborn mortality and morbidity;
2. allows the reduction of the risk of GDM in women with a history of GDM in anamnesis;
3. prevents the transmission of DM and metabolic disorders from one generation to another.

Prevention of GDM

GDM is not totally preventable, but there are ways to help lower the risk!

Environmental risk factors must be considered in the prevention of GDM. Control and elimination of environmental and socioeconomic risk factors comprise the population strategy and are the responsibility of the State and Government.[18]

A high-risk strategy is aimed at the elimination of risks existing in the high-risk population. Influencing reversible individual risk factors, such as obesity and waist circumference. Unhealthy diet, physical inactivity, smoking, etc., are primarily the responsibility of each individual.

According to the 2019 Research Trusted Source, the ideal time to influence individual risk factors is around pregnancy.[32]

Measures to reduce the potential risks of GDM development include:

- Elimination of reversible individual risks means:
- Maintenance of healthy body weight;
- In case of overweight, losing 5-7% of body weight;
- Once pregnant, a woman should not lose weight unless it is needed;
- If a woman's condition allows, performing regular physical activity;
- During pregnancy, walking and swimming are good and safe;
- Inclusion of fiber in each meal (vegetables, greens, fruit)
- Limiting sweets (especially from beverages and desserts)
- Blood sugar testing as early as three months before conception, if a woman has a history of GDM and she is planning pregnancy;
- Planning of each subsequent pregnancy, if a woman had GDM in a prior pregnancy;
- If GDM risk factors are present, then screening tests should be performed in the first trimester to see if the condition has developed again

The best time to lower the risk of GDM and make lifestyle changes is during family planning or a long time before getting pregnant!

Treatment of GDM

If GDM is revealed during screening, treatment should be initiated immediately. Treatment of GDM includes:

- Special meal plans;
- Scheduled physical activity;
- Daily blood glucose testing (in GDM);
- Insulin injections (in GDM, if needed);
- Metformin (if needed).[33]

Conclusion

Aggressive influence of risk factors, mainly reversible environmental, socio-economic, and individual ones, has led to a critical increase in GDM prevalence in high-, middle-, and low-in-

come countries. GDM that is not diagnosed, or is diagnosed late, or if proper treatment is not provided, shows high feto-maternal morbidity and mortality.

Timely and correct screening is essential for the prevention of GDM complications and fetal programming in adult life.

Though GDM cannot be totally prevented, a lot can be done to lower the risk, as what happens in the womb lasts all life!

Financial Disclosure: None reported.

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