

# Gestational Diabetes Mellitus: Risk and its Challenges

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## Abstract

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance that was not present or recognized prior to pregnancy. GDM is associated with adverse outcome for mother and fetus. The prevalence of GDM varies from 1-14% and depends on population studied and diagnostic criteria used. This mini review discusses about the various aspects of GDM like aetiology, epidemiology, pathophysiology, diagnosis and management.

**Keywords:** Gestational Diabetes Mellitus (GDM); Pathophysiology; Diagnosis; Management

## Introduction

Diabetes mellitus (DM) is a complex metabolic disorder which is characterized by a hyperglycemic condition. According to the World Health Organization (WHO), diabetes mellitus (DM) is classified into four broad categories: DM type 1, DM type 2, other rare types of DM (such as genetic defects of  $\beta$ -cell function or insulin action, diseases of the exocrine pancreas and drug induced DM) and Gestational diabetes mellitus (GDM) [1]. Gestational diabetes mellitus (GDM) occurs when a woman's pancreatic function is not sufficient to overcome the diabetogenic environment of pregnancy. Among various metabolic complications of pregnancy GDM is one of them as it is associated with adverse outcome for the mother, the fetus, neonate, child and adult offspring of the diabetic mother. Gestational diabetes mellitus (GDM) is defined as glucose intolerance that was not present or recognized prior to pregnancy. It can also be defined as "carbohydrate intolerance of variable severity with onset or first recognition during pregnancy". The definition is applicable regardless of whether insulin is used for treatment or the condition persists after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated the pregnancy [2,3]. Historical information related to GDM is presented in Table 1.

## Epidemiology

The prevalence rate of GDM varies from 1% to 14% of all pregnancies and depends on the population studied and the diagnostic tests employed [4]. GDM complicates up to 14% of all pregnancies, resulting in approximately 200,000 cases annually in the United States [2]. It is a major cause of perinatal morbidity and mortality, as well as maternal long-term morbidity. The prevalence in the United Kingdom

and among European countries was estimated to be 5%, 2-6% respectively. Higher prevalence of GDM was noted in African, Asian, Indian and Hispanic women [4]. In the United States, prevalence rates for GDM are higher for African American, Hispanic, American Indian, and Asian women than for white women. Incidence rates of GDM, in India, are estimated to be 10-14.3% which is much higher than the west and is expected to increase to 20% i.e., one in every 5 pregnant women is likely to have GDM [5]. Of all types of diabetes, GDM accounts for approximately 90-95% of all cases of diabetes in pregnancy.

## Aetiology

Several risk factors are associated with the development of GDM which include advanced maternal age, maternal obesity, high parity, previous delivery of a macrosomic infant, family history of type 2 diabetes mellitus, maternal short stature, polycystic ovary disease, high levels of saturated fat in the diet, prior GDM, prior neonatal death, prior cesarean delivery, previous stillbirth or congenital malformations, high blood pressure during pregnancy, multiple pregnancy [2]. No known risk factors are identified in 50% of patients with GDM.

## Pathophysiology

The main factor underlying behind the causation of GDM is insufficient insulin levels. Three regions can be attributed for this:

- 1) Autoimmune cell dysfunction.
- 2) Highly penetrant genetic abnormalities that lead to impaired insulin secretion.
- 3) Cell dysfunction that is associated with chronic insulin resistance [6].

Impaired insulin secretion and insulin resistance during pregnancy arise from a variety of factors, including alterations in growth hormone and cortisol secretion human placental lactogen and insulinase secretion. In addition, estrogen and progesterone also contribute to a disruption of the glucose insulin balance [7]. However, the detailed genetic and molecular mechanism causing pancreatic cell dysfunction that lead to insulin insufficiency in GDM are not fully revealed yet.

Year	Event
1893	Bennewitz first gave the reference of diabetes in Pregnancy
1949	Priscilla White published the first version of the classification system of GDM
1952	Jorgan pedersen proposed his hyperglycemia [maternal] hyperinsulinism [fetal] hypothesis which is later called as Pederson theory
1979	White classification underwent its last version
1964	O' Sullivan proposed criteria to interpret glucose tolerance level in pregnancy to identify women at a higher risk for developing diabetes after delivery
1979	Criteria proposed by O' Sullivan was modified by National Diabetes Data Group [NDDG]
2008	HAPO study was published which gives valuable information regarding the risks of adverse outcomes associated with various degrees of maternal glucose intolerance.

**Table 1:** Different event related to Gestational Diabetes Mellitus (GDM).

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### Screening and Diagnosis of GDM

The screening and diagnosis of gestational diabetes mellitus (GDM) continues to be a contentious issue. International bodies lack consensus on a uniform global approach to screening and diagnosis of GDM. Guidelines for screening and diagnosis of GDM vary among countries and between major societies worldwide etc. Different criteria proposed by different bodies for screening of GDM have been presented in Table 2. Each of these criteria has some drawbacks. In order to remove the discrepancy involved in diagnostic testing the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study was planned. and data generated by HAPO study was used by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) panel to develop a single step 75 g OGTT to be done in all pregnant women at 24–28 weeks of gestation which is now accepted by various scientific bodies [8]. Criteria proposed by IADPSG are given in Table 3.

### Complications

The short-term complications for a mother with GDM include pre-eclampsia, polyhydramnios, cesarian section, pyelonephritis, asymptomatic bacteriuria, and urinary tract infections. Similarly, the main short-term complications for the fetus-neonate include perinatal mortality, macrosomia, obstetric trauma, hypoglycemia, hyperbilirubinemia and hypocalcemia. While the long term complications GDM mother may be vulnerable to develop diabetic retinopathy, diabetic nephropathy and type 2 diabetes [1,4].

### Management/Treatment of GDM

The cornerstone of management is glycemic control. The aim of treatment is to maintain maternal blood concentration within an acceptable range in a normal pregnancy. Proper management of GDM includes Medical Nutrition Therapy (MNT), exercise

and pharmacological treatment. These all can be applied either in combination or alone depending on the individual body response. Pharmacological treatment includes insulin therapy and oral hypoglycemic agents like metformin, glyburide, acarbose and glibenclamide. Management reduces rates of adverse pregnancy outcomes including perinatal mortality, neonatal hypoglycemia, neonatal hyperbilirubinemia, elevated cord blood C-peptide level, and birth trauma.

### Discussion and Conclusion

GDM is defined as “carbohydrate intolerance of variable severity with onset or first recognition during pregnancy”. The prevalence rate of GDM may range from 1-14%. It is highly prevalent among African, Asian, Indian and Hispanic women. Of all the diabetes associated with pregnancy, GDM contributes to 90-95% of it. The prevalence rate has increased in recent years. It is believed that factors are responsible for development of GDM like age, obesity, lifestyle and previous history of diabetes. GDM may lead to significant maternal and fetal complications if it is left untreated. Hence, the impact of GDM on maternal and infant health is of great clinical and public health concern and need to focus on management of GDM induced complications in near future. It is also compulsory for all the pregnant women to undergo random blood glucose at the first antenatal visit to detect diabetes in pregnancy. The mechanism of GDM development is not fully understood, though with proper management it can be prevented, and thus infant mortality and morbidity can be checked. A wide study is required on all the aspects of GDM.

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Criteria	Year	Approach	Glucose load
O'Sullivan and Mahan	1964	2 Step	100
National Diabetes Data Group (NDDG)	1979	2 Step	100
Carpenter and Coustan	1982	2 Step	100
World Health Organization (WHO)	1999	1 Step	75
American Diabetes Association (ADA)	2004	2 Step	100
Latin American Diabetes Association (ALAD)	2008	2 Step	75
International Association of Diabetes and Pregnancy Study Groups (IADPSG)	2010	1 Step	75
World Health Organization 2013 criteria (revised, same as IADPSG)	2013	1 Step	75
National Institute for Health and Care Excellence (NICE)	2015	1 Step	75

Table 2: Various criteria proposed for diagnosing GDM based on fasting OGTT [7].

First prenatal visit	Measure FPG, HbA1c or RPG	Overt diabetes if, FPG ≥ 126 mg/dl (7.0 mmol/l)
		Or random plasma glucose ≥ 200 mg/dl (11.1 mmol/l)
		Or HbA1c ≥ 6.5%
		GDM if, FPG ≥ 92 mg/dl (5.1 mmol/l) but <126 mg/dl (7.0 mmol/l)
If the test is normal in the first prenatal visit, test for GDM during 24–28 weeks		
24–28 weeks of gestation	75 g OGTT	Pre-existing diabetes if
		FPG ≥ 126 mg/dl (7.0 mmol/l)
		GDM if, FPG ≥ 92 mg/dl (5.1 mmol/l)
		1 h ≥ 180 mg/dl (10.0 mmol/l)
		2 h ≥ 153 mg/dl (8.5 mmol/l)

Table 3: IADPSG criteria for diagnosis of GDM and overt diabetes in pregnancy [7].