

For the Primer, visit doi:10.1038/s41572-019-0098-8

→ Gestational diabetes mellitus (GDM) is the most common complication in pregnancy. GDM involves the development of gestational hyperglycaemia that resolves immediately after birth but carries short-term and long-term health risks for both mother and baby.

PATHOPHYSIOLOGY

DIAGNOSIS

Consensus is lacking on a single protocol or set of criteria to diagnose GDM. The multinational HAPO study showed that mild maternal hyperglycaemia was linearly associated with adverse maternal outcomes (such as pre-eclampsia) and fetal outcomes (such as neonatal adiposity and shoulder dystocia). Threshold glucose values were subsequently selected based on the risk of these hyperglycaemia-related pregnancy complications. The International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria — namely, hyperglycaemia diagnosed in pregnancy that does not exceed that in overt diabetes outside of pregnancy — are most widely accepted, although they are not commonly used in the United States, Canada or the United Kingdom. The IADPSG-recommended diagnostic protocol involves a ‘one-step’ method: a fasting oral glucose tolerance testing (OGTT) at 24–28 weeks of gestation. However, a ‘two-step’ method that includes a prescreening step (a non-fasting, glucose challenge test (GCT)), to determine the need for an OGTT, is preferred in some parts of the world. Although the two-step method reduces the diagnostic burden for patients, it can lead to underdiagnosis of GDM.



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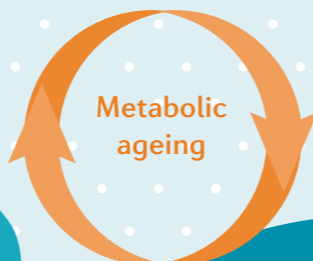
EPIDEMIOLOGY

The lack of consensus and uniformity in GDM diagnostic criteria complicates comparison of prevalence between countries. Nevertheless, prevalence estimates of 1.8–31% have been reported. The major risk factors for

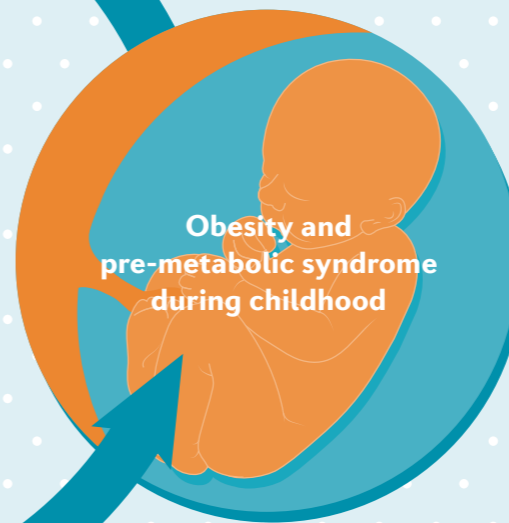
developing GDM include diet and lifestyle factors (such as overweight and obesity), later age at childbearing, previous history of GDM, family history of type 2 diabetes mellitus (T2DM) and ethnicity. Emerging risk factors include

environmental factors (such as endocrine disruptors) and psychosocial factors (such as depression). Genetic factors, such as polymorphisms in genes involved in the regulation of insulin secretion, also modify GDM risk.

Increased insulin resistance and metabolic inflammation during pregnancy



Adult metabolic syndrome, T2DM and obesity



Fetal–neonatal metabolic programming of obesity

Rx MANAGEMENT

Treatment of GDM aims to prevent pregnancy complications and fetal overgrowth. Lifestyle interventions are the mainstay of treatment, including dietary modifications (a low-glycaemic-index diet and limiting gestational weight gain) and physical activity (such as walking, cycling and swimming). If lifestyle interventions are ineffective at lowering hyperglycaemia after ≥1–2 weeks, then pharmacological therapy with insulin, metformin or glibenclamide is initiated. Prevention of long-term maternal complications, such as T2DM and cardiovascular disease, requires extending lifestyle interventions and, if necessary, pharmacotherapy beyond pregnancy.



OUTLOOK

Improved identification of problematic glucose levels in pregnancy and prognosis should be aided by biomarker research and the development of a simpler, non-fasting alternative to the complex OGTT. Further research to increase understanding of GDM pathophysiology should facilitate targeted intervention to improve short-term and long-term outcomes in offspring. The rising incidence of hyperglycaemia and obesity in the general population are challenges for prevention of GDM, and will probably require preventative efforts at the population level to optimize the health of both parents before conception.