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Gestational diabetes: Current trends in treatment and long-term complications

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***Abstract*---Background:** Gestational diabetes mellitus (GDM) is characterized by carbohydrate intolerance first recognized during pregnancy. Its prevalence varies globally, influenced by diagnostic criteria and demographic factors, with recent estimates indicating that one in seven live births worldwide is affected. Rising obesity rates, sedentary lifestyles, and advancing maternal age contribute to this trend. **Aim:** This article reviews current trends in GDM treatment and examines long-term complications for both mothers and offspring. **Methods:** A comprehensive literature review was conducted, encompassing guidelines from major health organizations and recent cohort studies on GDM screening, diagnosis, management, and outcomes. **Results:** The review identified variations in screening practices across guidelines, with consensus recommending universal screening during the second trimester, though early screening in high-risk populations is increasingly advocated. GDM management strategies include dietary interventions, physical activity, and insulin

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therapy as needed. Long-term studies indicate that women with a history of GDM face increased risks of developing type 2 diabetes, while offspring are at higher risk for obesity and metabolic syndrome. **Conclusion:** Given the rising incidence of GDM and its potential long-term complications, tailored screening and management strategies are essential. Ongoing research into the pathophysiology and effective interventions will enhance outcomes for affected individuals.

***Keywords*---**gestational diabetes, screening, management, long-term complications, type 2 diabetes, obesity.

Introduction

Gestational diabetes mellitus (GDM) is conventionally characterized as a form of carbohydrate intolerance of varying degrees, which first occurs or is detected during pregnancy [1]. This classification includes impaired glucose tolerance that resolves postpartum and diabetes mellitus (DM) that was either undiagnosed before or developed during pregnancy. The latter category includes type 2 diabetes mellitus (T2DM), with rarer cases of type 1 diabetes mellitus (T1DM) or monogenic diabetes (see Glossary) [2]. A more contemporary definition of GDM, "diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation," has been proposed to enhance diagnostic clarity [3]. The prevalence of GDM differs significantly based on population demographics and the diagnostic criteria employed. Cohort studies conducted in the UK and Ireland before 2010 indicated that 1–3% of pregnancies were affected by GDM [4]. In contrast, the prevalence ranged from 9% to 26% (average 18%) at 15 centers participating in the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study when stricter diagnostic standards were applied [5]. In 2017, it was estimated that one in seven live births globally was impacted by GDM [6], representing 85% of the total 21.3 million live births influenced by diabetes during pregnancy worldwide [6]. Key contributors to the increasing incidence of GDM include the obesity epidemic, sedentary lifestyles, and advanced maternal age [7]. Despite GDM being one of the most prevalent pregnancy complications, considerable debate persists regarding screening timelines, diagnostic thresholds, optimal management, and postpartum follow-up.

Early Screening in Pregnancy

Early screening, typically conducted in the first trimester or at the initiation of prenatal care, is commonly recommended to rule out pre-existing DM in high-risk women [2,3,8–10]. However, there is no consensus on the most appropriate early screening tool for pre-existing DM. Fasting plasma glucose, random plasma glucose, HbA1c, and the 75-g 2-hour oral glucose tolerance test (OGTT) are all recommended by various national guidelines as screening options [2,3,8,10–12]. Results indicative of DM based on World Health Organization (WHO) criteria outside pregnancy (i.e., fasting glucose ≥ 7 mmol/l, 2-hour 75-g OGTT, or random glucose ≥ 11.1 mmol/l, or HbA1c ≥ 48 mmol/mol) should be considered indicative of "diabetes in pregnancy," necessitating appropriate management [9]. Whether GDM can be diagnosed in the first trimester, as opposed to the second or third

trimester, remains a subject of debate. The International Association of Diabetes in Pregnancy Study Groups (IADPSG) retracted their 2010 recommendation that fasting plasma glucose ≥ 5.1 mmol/l in early pregnancy be considered diagnostic of GDM, following evidence showing it was a poor predictor of OGTT outcomes in the third trimester [8,13]. For example, a retrospective cohort study in China involving data from 17,186 pregnant women found that 37% of those with fasting plasma glucose between 5.10 and 5.59 mmol/l at their first antenatal visit were later diagnosed with GDM based on a 75-g OGTT between 24 and 28 weeks of gestation [14]. Ongoing studies are assessing the diagnostic value of conducting an OGTT between 12 and 15 weeks and 18 and 20 weeks of gestation [15,16].

Guideline Recommendations for Early Pregnancy Diabetes Mellitus Screening

The International Association of Diabetes in Pregnancy Study Groups (IADPSG) recommends screening for either all pregnant women or those at high risk, with the decision being influenced by local conditions and the prevalence of abnormal glucose tolerance in the population. This flexible approach allows for adjustment based on local circumstances, including healthcare infrastructure and population-specific risk factors [8]. The World Health Organization (WHO) advises that screening protocols be tailored by individual countries or health services, depending on the prevalence of glucose intolerance, resource availability, and other competing health priorities within the population. This recommendation reflects a need for context-specific approaches that prioritize national healthcare needs [9].

The American Diabetes Association (ADA) suggests that screening be conducted for women with one or more risk factors for diabetes mellitus (DM). Risk factors include a first-degree relative with DM, high-risk racial or ethnic backgrounds, a history of cardiovascular disease, hypertension (140/90 mmHg or taking antihypertensive therapy), HDL cholesterol levels below 35 mg/dl (0.9 mmol/l), or triglyceride levels above 250 mg/dl (2.82 mmol/l). Additionally, conditions such as polycystic ovarian syndrome (PCOS), physical inactivity, or other clinical conditions associated with insulin resistance (e.g., acanthosis nigricans, severe obesity) warrant screening. Women with a history of gestational diabetes mellitus (GDM) are recommended to undergo screening for diabetes every three years [3].

The American College of Obstetricians and Gynecologists (ACOG) advises screening overweight or obese women (with a BMI of 25 kg/m² or 23 kg/m² for Asian Americans) if they also have one or more additional risk factors. These risk factors include physical inactivity, a first-degree relative with DM, a history of macrosomia (baby over 4 kg), previous GDM, hypertension, low HDL cholesterol (<35 mg/dl), high triglycerides (>250 mg/dl), PCOS, HbA1c levels of 5.7% or higher, or a history of impaired glucose tolerance or fasting glucose on previous tests. Additional factors include clinical conditions linked to insulin resistance (e.g., acanthosis nigricans, pre-pregnancy BMI over 40 kg/m²), and a history of cardiovascular disease [11].

The Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Health and Care Excellence (NICE) suggest screening individuals with one or

more risk factors for DM. These risk factors include a BMI greater than 30 kg/m², a previous macrosomic baby weighing over 4.5 kg, a history of GDM, a first-degree relative with DM, or family origins associated with a high prevalence of DM [2,10]. Diabetes Canada recommends screening for women who are at high risk of having undiagnosed type 2 diabetes mellitus (T2DM), thereby identifying women who may have been missed in routine screening protocols [12].

Screening Later in Pregnancy

Screening for gestational diabetes mellitus (GDM) typically occurs between 24 and 28 weeks of gestation via an oral glucose tolerance test (OGTT). A "one-step" 2-hour 75-gram OGTT is recommended by organizations such as the IADPSG, WHO, and various national guideline bodies [2,3,8–10]. However, an alternative "two-step" method, which involves a glucose challenge test followed by an OGTT for those with a positive result, is also advocated. This method is either recommended as an alternative by the American Diabetes Association (ADA) or preferred by bodies such as the American College of Obstetricians and Gynecologists (ACOG) and Diabetes Canada for use in the US and Canada [3,11,12]. While universal screening in the third trimester is supported by several organizations (IADPSG, ADA, ACOG, Diabetes Canada), guidelines in the UK suggest restricting screening to women who present clinical risk factors for GDM [Scottish Intercollegiate Guidelines Network (SIGN), National Institute for Health and Care Excellence (NICE)] [2,3,8,10–12].

Diagnostic Criteria and Thresholds

The diagnostic thresholds for GDM have evolved over recent decades and remain a subject of ongoing debate. The IADPSG Consensus Panel updated its diagnostic criteria in 2010, based on the findings of the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study, which have been widely endorsed by both national and international bodies [8]. The HAPO study, an international cohort study that included over 25,000 women from diverse backgrounds, established a strong and continuous link between maternal glucose levels and key outcomes, such as increased birth weight [17]. This relationship included glucose levels below the diagnostic threshold for diabetes, which were previously not recognized as harmful. GDM diagnostic thresholds were set somewhat arbitrarily at glucose values associated with an estimated 1.75 odds ratio for birth weight, cord C-peptide levels, and infant body fat percentages above the 90th percentile, relative to mean glucose values for the study cohort [8]. Following the adoption of IADPSG criteria, the prevalence of GDM tripled or quadrupled at two European centers compared to the previous two-step ADA (Carpenter-Coustan) screening method [18,19].

Glucose Regulation During Pregnancy

Several changes in glucose regulation occur during pregnancy to support the nutrient demands of the developing fetus. Studies using hyperinsulinemic-euglycemic clamps in healthy lean women show that insulin sensitivity decreases by 56%, and basal endogenous glucose production increases by 30% in the third trimester compared to pre-pregnancy [20,21]. In women with normal glucose

tolerance, pancreatic beta cells adapt by producing more insulin, thus maintaining normal blood glucose levels. For instance, first- and second-phase insulin responses to an intravenous glucose tolerance test increased approximately threefold in late pregnancy compared to pre-pregnancy in a small study of normal controls [22]. Insulin resistance associated with pregnancy resolves within days postpartum, as demonstrated by glucose clamp studies, suggesting that these changes are mediated by placental factors [23].

Pathophysiology of GDM

GDM is characterized by an insufficient pancreatic beta-cell response to the heightened insulin demands of pregnancy, leading to varying degrees of hyperglycemia. The key pathophysiological features of insulin resistance and defective insulin secretion in GDM resemble those observed in type 2 diabetes mellitus (T2DM). Studies by Catalano et al., particularly through hyperinsulinemic-euglycemic clamp studies, have extensively examined GDM pathophysiology. These studies revealed significantly reduced insulin sensitivity in women with GDM compared to control subjects, persisting throughout pregnancy and even before conception [24]. A reduction in insulin sensitivity of approximately 50–60% in late pregnancy, relative to pre-pregnancy levels, was observed in women with GDM and in those with normal glucose tolerance [22,25]. Thus, pregnancy may reveal previously unrecognized beta-cell dysfunction by exacerbating pre-existing insulin resistance.

The Role of Obesity

GDM shares several non-modifiable risk factors with T2DM, including advanced maternal age, family history of diabetes, and ethnicities with a higher prevalence of diabetes (e.g., South Asian, Middle Eastern, and Black Caribbean) [26]. Obesity, however, stands out as the most significant modifiable risk factor for GDM, posing a public health challenge given its rising global prevalence [27]. These genetic and environmental risk factors suggest the involvement of complex mechanistic pathways in the development of GDM. A meta-analysis of 20 cohort studies from North America, Europe, and Australia estimated that the risk of developing GDM is two, four, and eight times higher in overweight, obese, and severely obese women, respectively, compared to women with normal body mass index (BMI) [27]. A population-based analysis of 23,904 women in the US provided stratified GDM prevalence data by BMI [28]. The population-attributable fraction of GDM associated with overweight and obesity was estimated to be 46% [95% CI 36–56%].

The notable occurrence of type 2 diabetes mellitus (T2DM) among women with a history of gestational diabetes mellitus (GDM) suggests the potential for a shared genetic pathway. Numerous genes that are critical to the development, functionality, and survival of pancreatic beta cells have been identified through genome-wide association studies (GWAS) as influencing the risk of T2DM. For instance, genetic variants at loci such as TCFL7, CDKAL1, and MTNR1B have been linked to an elevated risk of T2DM in populations of varying ethnic backgrounds [29]. Mutations in TCF2, a transcription factor encoding hepatic nuclear factor 1b, were originally identified in a subtype of monogenic diabetes.

However, the role of TCF2 variations in T2DM remains unclear, with some GWAS reporting both reduced and increased risks across different ethnic groups [30,31].

A Danish cohort study examined the prevalence of 11 genetic loci associated with increased susceptibility to T2DM among women with previous GDM (n = 283) and middle-aged controls with normal glucose tolerance (n = 2446) [32]. When age and BMI were accounted for, three susceptibility alleles were significantly linked to a heightened risk of GDM: TCF7L2 rs7903146 [odds ratio (OR) 1.44, 95% CI 1.19–1.74, P = 0.00017], CDKAL1 rs7756992 [OR 1.22, 95% CI 1–1.49, P = 0.049], and TCF2 rs7501939 [OR 1.22, 95% CI 1.01–1.48, P = 0.039]. A significant cumulative effect was also observed when more than one of these alleles was present, further increasing the risk of GDM (OR 1.18, 95% CI 1.10–1.27 per allele, $P = 3.2 \times 10^{6}$).

Subsequent research conducted in Finland assessed 69 single nucleotide polymorphisms (SNPs) associated with T2DM in women with prior GDM (n = 533) and control subjects with normal glucose tolerance (n = 407) [33]. Age-adjusted analyses revealed several risk variants, with the strongest association found for two MTNR1B SNPs: rs10830963 (OR 1.62, 95% CI 1.34–1.96, $P = 1.3 \times 10^{7}$) and rs1387153 (OR 1.38, 95% CI 1.14–1.66, $P = 3.6 \times 10^{4}$). Additional SNPs, including TCF7L2 rs7903146 (OR 1.3, 95% CI 1.03–1.64, P = 0.016) and GCKR rs780094 (OR 1.25, 95% CI 1.03–1.51, P = 0.028), were also nominally associated with an increased risk of GDM.

Further investigations into the impact of two risk variants, TCF7L2 rs7903146 and GCK rs1799884, were conducted in a cohort comprising 3811 European and 1706 Thai participants from the HAPO study [34]. In the European subgroup, TCF7L2 rs7903146 showed a significant association with elevated blood glucose levels at fasting, 1 hour, and 2 hours during an oral glucose tolerance test (OGTT) at 24–32 weeks' gestation (fasting 0.02 mmol/l increase per T-allele, 95% CI 0.002–0.03, P = 0.03; 1-hour glucose 0.16 mmol/l increase per T-allele, 95% CI 0.08–0.24, P < 0.0001; 2-hour glucose 0.13 mmol/l increase per T-allele, 95% CI 0.07–0.19, P < 0.0001). No significant associations were observed in the Thai subgroup. TCF7L2 rs7903146 was also linked to higher odds of GDM diagnosis based on IADPSG criteria in the European group (per T-allele OR 1.15, 95% CI 1.00–1.31, P = 0.04), whereas GCK rs1799884 was associated with increased odds of GDM diagnosis in both European and Thai subgroups (European OR 1.29, 95% CI 1.09–1.50, P = 0.001; Thai OR 1.42, 95% CI 1.06–1.77, P = 0.007).

To date, the only GWAS on GDM was conducted in the Korean population, revealing strong associations between GDM and the risk alleles MTNR1B rs10830962 (OR 1.454, 95% CI 1.315–1.608, $P = 2.49 \times 10^{13}$) and CDKAL1 rs7754840 (OR 1.518, 95% CI 1.372–1.680, $P = 6.65 \times 10^{16}$) [35].

Diagnosis of Gestational Diabetes:

Diagnostic thresholds for gestational diabetes mellitus (GDM) using the oral glucose tolerance test (OGTT) at 24–28 weeks of gestation have been established by various organizations, with slight variations in their criteria. According to the guidelines set by the International Association of Diabetes and Pregnancy Study

Groups (IADPSG), the World Health Organization (WHO), the American Diabetes Association (ADA), Diabetes Canada, and the Scottish Intercollegiate Guidelines Network (SIGN), a 75-gram glucose load is recommended. The fasting glucose level threshold is 5.1 mmol/L (92 mg/dL), the 1-hour glucose level is 10.0 mmol/L (180 mg/dL), and the 2-hour glucose level is 8.5 mmol/L (153 mg/dL) [2,3,8,9,12].

The National Institute for Health and Care Excellence (NICE) also recommends a 75-gram glucose load, but its criteria are slightly different. For fasting glucose, the threshold is 5.6 mmol/L (101 mg/dL), and the 2-hour glucose level is set at 7.8 mmol/L (140 mg/dL) [10]. In contrast, the ADA's Carpenter-Coustan criteria, which use a 100-gram glucose load, have fasting, 1-hour, 2-hour, and 3-hour thresholds set at 5.3 mmol/L (95 mg/dL), 10.0 mmol/L (180 mg/dL), 8.6 mmol/L (155 mg/dL), and 7.8 mmol/L (140 mg/dL), respectively [3].

The National Diabetes Data Group (NDDG) guidelines, also adopted by the ADA, use a 100-gram glucose load and set higher thresholds: 5.8 mmol/L (105 mg/dL) for fasting, 10.6 mmol/L (190 mg/dL) for 1-hour, 9.2 mmol/L (165 mg/dL) for 2-hour, and 8.0 mmol/L (145 mg/dL) for 3-hour glucose levels [3]. Additionally, Diabetes Canada recommends a 75-gram glucose load with fasting glucose levels at 5.3 mmol/L (95 mg/dL), a 1-hour glucose level of 10.6 mmol/L (190 mg/dL), and a 2-hour glucose level of 9.0 mmol/L (162 mg/dL) [12].

Intrauterine Environment

Epidemiological studies indicate that offspring risk for Type 2 diabetes mellitus (T2DM) is more strongly linked to maternal diabetes compared to paternal diabetes. For example, an American cohort study showed that 33% of women with gestational diabetes mellitus (GDM) reported a maternal history of diabetes, while only 12% of women with pregestational diabetes reported the same ($P < 0.001$) . Additionally, longitudinal data from the Framingham Heart Study found that offspring with one diabetic parent had a 3.5-fold higher risk of T2DM, and those with both diabetic parents had a 6-fold increased risk . The risk was particularly elevated when maternal diabetes occurred before age 50 (OR 9.7, 95% CI 4.3–22.0).

Beyond genetics, the intrauterine environment seems to contribute significantly to this risk. A study of Pima Indian families highlighted that siblings born after maternal T2DM diagnosis had a higher diabetes risk compared to those born before the diagnosis (OR 3.7, 95% CI 1.3–11.3, $P = 0.02$), with no similar effect observed in relation to paternal diabetes . GDM also creates a proinflammatory fetal environment, marked by elevated levels of cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) , which may influence fetal epigenetic modifications, potentially increasing diabetes susceptibility later in life . Further mechanistic studies are needed to fully elucidate the interplay between these factors.

Complications of Hyperglycemia and Gestational Diabetes Mellitus (GDM)

Maternal and Fetal Complications: Elevated blood glucose levels during pregnancy are closely linked to numerous unfavorable outcomes for both the mother and the fetus. The pivotal Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study established a definitive linear connection between mild dysglycemia, even in the absence of overt diabetes mellitus (DM), and short-term negative pregnancy outcomes. Subsequent research has consistently supported these conclusions, indicating that gestational diabetes mellitus (GDM) is associated with a variety of both short- and long-term health risks for mothers and their offspring (HAPO study [17]).

Offspring Complications: Infants born to mothers with GDM are at higher risk of several immediate complications, including:

- Excessive fetal growth (macrosomia)
- Preterm delivery
- Birth-related injuries such as shoulder dystocia
- Low blood sugar levels in the newborn (neonatal hypoglycemia)
- Admission to neonatal care units
- Respiratory distress syndrome (RDS) (HAPO study [17], [47–51]).

Maternal Complications

Women with gestational diabetes mellitus (GDM) are at an elevated risk for several serious perinatal complications, including gestational hypertension, pre-eclampsia, polyhydramnios, Caesarean section, and shoulder dystocia [17,47,48,50,51]. The likelihood of GDM recurrence in a subsequent pregnancy was estimated to be 48% in a meta-analysis of 18 studies [58]. Recurrence of GDM was observed more frequently in non-white European ethnic groups (such as Hispanic, African American, and Asian) and multiparous women. Additional risk factors for GDM recurrence include obesity, advanced maternal age, and early gestation at the time of diagnosis during the initial pregnancy [59]. Furthermore, women who previously experienced GDM have a sevenfold increased risk of developing type 2 diabetes mellitus (T2DM) compared to women with normal glucose tolerance during pregnancy, as shown in a meta-analysis [60]. Research estimates that up to one-third of T2DM cases among parous women are preceded by GDM [61]. A systematic review of 28 studies revealed that the cumulative incidence of T2DM escalates rapidly within the first five years following the index pregnancy, reaching a plateau beyond ten years of follow-up [62]. The observed cumulative incidence of T2DM ranged from 2.6% to 70% across follow-up periods extending from six weeks to 28 years postpartum. In adjusted analyses accounting for differences in T2DM screening rates and follow-up durations, five studies reported a cumulative incidence of 50% or greater within 5–10 years following the index pregnancy. Interestingly, the cumulative incidence appeared similar across different ethnic groups after adjusting for interstudy variability. A higher fasting glucose level on an oral glucose tolerance test (OGTT) was identified as the most significant factor linked to GDM progression to T2DM, although determining a specific risk threshold proved difficult due to variations in statistical analyses across studies [62]. Generally, increasing maternal body mass index (BMI), early gestational age at GDM

diagnosis, and impaired glucose tolerance postpartum have been identified as predictors for future T2DM development [57].

Treatment

The primary objective of GDM treatment is to correct hyperglycemia and minimize the risk of associated adverse pregnancy outcomes. The beneficial effects of medical intervention on both fetal and maternal morbidity were first demonstrated in the landmark Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) [63]. Intervention strategies including dietary guidance, blood glucose monitoring, and insulin therapy (if necessary) were associated with a 67% reduction in the primary composite outcome of infant death, shoulder dystocia, bone fractures, and nerve palsy when compared with usual care. Furthermore, reductions in average birthweight and incidences of macrosomia were also noted. Similar positive outcomes were observed in the Maternal-Fetal Medicine Units Network randomized trial, conducted in 958 women diagnosed with 'mild' GDM (i.e., normal fasting glucose levels on OGTT). This intervention, which included a similar treatment package, was linked to reductions in clinical outcomes such as macrosomia, Caesarean delivery, shoulder dystocia, and pre-eclampsia when compared to standard care (Table 4) [64]. The management of GDM should be conducted within a multidisciplinary framework involving both diabetes and obstetric care. Education on lifestyle modifications and capillary blood glucose monitoring should be provided by diabetes specialist nurses and dieticians. National guidelines recommend fasting and postprandial (either one or two hours after meals) capillary blood glucose monitoring [2,10,12,65].

Glucose monitoring targets differ across guidelines but are influenced by those established in the ACHOIS and Maternal-Fetal Medicine Units Network trials[65]. **Lifestyle Intervention** is crucial in managing gestational diabetes mellitus (GDM) and typically includes modifications in diet, physical activity, and weight management. It is estimated that such interventions alone may help achieve blood glucose targets in approximately 70–85% of women diagnosed using the American Diabetes Association (ADA) criteria[65]. Individualized targets for gestational weight gain should be established to optimize outcomes for both mother and fetus. The Institute of Medicine recommends weight gain targets based on pre-pregnancy body mass index (BMI), although specific recommendations for GDM are lacking[66].

A recent meta-analysis of randomized controlled trials indicated that dietary interventions are linked to improvements in mean maternal fasting glucose levels (13 studies; mean difference of 4.07 mg/dl, 95% CI 7.58 to 0.57, P = 0.02) and postprandial glucose levels (9 studies; mean difference of 7.78 mg/dl, 95% CI 12.27 to 3.29, P = 0.0007) when compared to control groups. These dietary changes also correlated with a reduced need for pharmacological treatment (RR 0.49, 95% CI 0.27–0.88, P = 0.02)[67]. Notably, there was a reduction in mean birthweight (decrease of 170.62 g, 95% CI 333.64 to 7.60, P = 0.04) and a lower incidence of macrosomia (RR 0.49, 95% CI 0.27–0.88, P = 0.02). A Cochrane review comparing lifestyle intervention with standard care or diet alone found that the intervention significantly decreased the risk of large-for-gestational-age

offspring (RR 0.6, 95% CI 0.5–0.71)[68]. Additional benefits from lifestyle interventions included a higher likelihood of achieving postpartum weight goals for mothers and a reduction in neonatal adiposity. Another Cochrane review investigated the effectiveness of combined diet and exercise interventions in preventing GDM, noting a trend towards reduced risk, though it did not reach statistical significance (RR 0.85, 95% CI 0.71–1.01)[69].

Pharmacological Therapy is warranted if blood glucose targets are unmet through lifestyle changes. In the United States and Canada, insulin is the first-line pharmacological treatment for GDM, whereas oral agents are preferred in the UK unless glucose levels are significantly elevated[2,10, 12, 65]. Insulin is usually administered via multiple daily injections, although continuous subcutaneous insulin infusion is also recognized as a viable option in U.S. guidelines [65]. Emerging evidence suggests that insulin analogues (both short and long-acting) are safe alternatives to human insulin during pregnancy[70]. Metformin and glibenclamide (known as glyburide in the U.S. and Canada) are the only oral agents recommended for GDM treatment. In the large, randomized Metformin in Gestational Diabetes (MiG) trial, no significant difference in perinatal complications (32.0% for metformin vs. 32.2% for insulin) or adverse events was observed between the two treatment groups[71]. However, 46% of participants on metformin required additional insulin to reach target glucose levels.

In another significant trial, glibenclamide and insulin demonstrated similar maternal and fetal perinatal outcomes, with only 4% of women on glibenclamide needing insulin to maintain acceptable blood glucose levels[72]. A randomized pilot study indicated that insulin may be more effective than glibenclamide as an adjunct therapy for women with GDM who do not meet glycemic targets with metformin monotherapy[73]. Insulin was associated with enhanced glycemic control and fewer instances of hypoglycemia compared to glibenclamide.
Meta-analyses evaluating the safety and efficacy of metformin versus glibenclamide have yielded mixed results. A 2015 meta-analysis suggested that metformin was linked to superior outcomes relative to glibenclamide, including less maternal weight gain, reduced birth weight, and lower rates of macrosomia[74]. However, this conclusion was based on only two randomized trials. A Cochrane review that assessed oral therapies for GDM across 11 trials concluded that there is insufficient evidence to definitively compare the benefits of specific oral therapies[75].

The long-term effects of fetal exposure to metformin and glibenclamide remain unclear. While glibenclamide appears to cross the placenta at low concentrations, concerns have been raised about its potential impact on placental glucose transporter expression, possibly resulting in increased fetal insulin production and long-term beta-cell fatigue[76]. Metformin crosses the placenta readily, with similar plasma levels found in both fetal and maternal circulation[77]. A recent case-control study analyzing data from 11 European congenital anomaly databases found no significant increase in the risk of all non-genetic congenital anomalies combined following metformin exposure in the first trimester of pregnancy[78]. However, an increased risk of pulmonary valve atresia (adjusted OR 3.54, 95% CI 1.05–12.00) after metformin exposure was reported, though the

authors noted this may represent a chance finding due to multiple statistical comparisons.

Conclusion

Gestational diabetes mellitus (GDM) presents significant challenges for maternal and neonatal health, with implications that extend beyond pregnancy. The increasing prevalence of GDM necessitates a comprehensive approach to screening, diagnosis, and management, particularly in light of the obesity epidemic and advancing maternal age. Early identification of women at high risk is crucial for implementing effective interventions that can mitigate adverse outcomes. Screening protocols vary significantly across different guidelines, leading to confusion in clinical practice. The recommendation for universal screening during the second trimester, while widely accepted, should be complemented by early screening for high-risk populations. Personalized screening strategies tailored to local demographic characteristics and healthcare resources could improve early diagnosis and management of GDM. Management strategies have evolved, emphasizing lifestyle interventions, including diet and exercise, alongside pharmacological options when necessary. Continuous education for healthcare providers and patients about the importance of lifestyle modifications during and after pregnancy is vital in reducing GDM incidence and its long-term effects. Longitudinal studies indicate that women with a history of GDM have a substantially higher risk of developing type 2 diabetes mellitus later in life, which underscores the need for postpartum screening and monitoring. Furthermore, the health implications for offspring born to mothers with GDM are concerning, with evidence suggesting an increased risk of obesity and metabolic disorders in childhood and adolescence. To address these challenges, multidisciplinary approaches that integrate obstetric, nutritional, and endocrinological care are essential. Future research should focus on the underlying mechanisms of GDM and its relationship with metabolic diseases, facilitating the development of targeted interventions. Furthermore, public health strategies should prioritize education and resources to support healthy lifestyles among pregnant women, ultimately aiming to decrease the burden of GDM and its long-term complications. In conclusion, the management of GDM requires a collaborative, evidence-based approach that acknowledges individual risk factors and aims to optimize health outcomes for mothers and their children. As our understanding of GDM continues to evolve, ongoing research and clinical vigilance are essential to improve care and mitigate the risks associated with this common pregnancy complication.

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سكري الحمل: الاتجاهات الحالية في العلاج والمضاعفات طويلة الأمد

الملخص:
خلفية :يُعرَف سكري الحمل (GDM) بأنه عدم تحمل الكربوهيدرات الذي يُكتشف لأول مرة أثناء الحمل. تختلف انتشاره عالميًا، متأثرةً بمعايير التشخيص والعوامل الديموغرافية، مع تقديرات حديثة تشير إلى أن واحدة من كل سبع ولادات حية في جميع أنحاء العالم تتأثر به. تسهم معدلات السمنة المتزايدة، وأنماط الحياة المستقرة، وزيادة عمر الأمهات في هذا الاتجاه.
الهدف :تستعرض هذه المقالة الاتجاهات الحالية في علاج سكري الحمل وتفحص المضاعفات طويلة الأمد لكل من الأمهات والأبناء.
الطرق :تم إجراء مراجعة شاملة للأدبيات، تشمل الإرشادات من المنظمات الصحية الكبرى والدراسات الحديثة حول فحص سكري الحمل، وتشخيصه، وإدارته، ونتائجه.
النتائج :حددت المراجعة اختلافات في ممارسات الفحص عبر الإرشادات، مع توافق ينصح بالفحص الشامل خلال الثلث الثاني من الحمل، على الرغم من أن الفحص المبكر في الفئات عالية الخطورة يُشجع عليه بشكل متزايد. تشمل استراتيجيات إدارة سكري الحمل التدخلات الغذائية، والنشاط البدني، والعلاج بالإنسولين حسب الحاجة. تشير الدراسات طويلة الأمد إلى أن النساء اللواتي لديهن تاريخ من سكري الحمل يواجهن مخاطر متزايدة لتطوير مرض السكري من النوع الثاني، في حين أن الأبناء معرضون لمخاطر أعلى للسمنة ومتلازمة الأيض.
الاستنتاج :نظرًا لزيادة حدوث سكري الحمل والمضاعفات المحتملة طويلة الأمد، فإن استراتيجيات الفحص والإدارة المخصصة ضرورية. ستعزز الأبحاث المستمرة في الفيزيولوجيا المرضية والتدخلات الفعالة النتائج للأفراد المتأثرين.
الكلمات المفتاحية :سكري الحمل، الفحص، الإدارة، المضاعفات طويلة الأمد، السكري من النوع الثاني، السمنة.