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Gestational Diabetes Mellitus: Prevalence, Management and Prevention

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Abstract

Gestational diabetes mellitus (GDM) is a significant health concern for pregnant women, associated with various adverse outcomes for both the mother and the fetus. This systematic review consolidates the current understanding and research on GDM, focusing on its prevalence, prevention, and treatment strategies. The review aims to highlight key findings and areas for future research, emphasizing the need for high-quality, inclusive studies to substantiate the effectiveness of various interventions. The review discusses the pathophysiology of GDM, the impact of maternal and neonatal adverse effects, and the comparison of treatment options such as insulin and metformin. Additionally, the study examines lifestyle interventions, dietary supplementation, and the use of probiotics as preventive measures. Accurate prevalence estimates are essential for the effective allocation of health resources and the development of prevention and management policies to address the rising rates of GDM. This review underscores the importance of standardized diagnostic criteria and screening strategies to obtain accurate and comparable prevalence estimates, ultimately aiming to improve maternal and neonatal health outcomes.

Key words: gestational diabetes mellitus, treatment, metformin, insulin

Introduction

Gestational diabetes mellitus (GDM) is a condition characterized by high blood sugar levels that are first identified during pregnancy. The management of GDM is crucial to prevent complications during pregnancy and ensure the health of both the mother and the fetus. GDM is associated with a range of adverse outcomes, including perinatal complications, an increased risk of developing diabetes and cardiovascular disease in the mother later in life, and a higher likelihood of childhood obesity in the offspring. The pathophysiologic basis of GDM involves relative insulin insufficiency, driven by the placenta's production of diabetogenic hormones such as human placental lactogen, leading to insulin resistance, particularly in late pregnancy. Risk factors for GDM include being overweight or obese, unhealthy dietary habits, physical inactivity, and advanced maternal age. GDM is one of the most frequent medical complications of pregnancy, affecting around 12-18% of pregnancies. The condition is usually diagnosed between 24 to 28 weeks of pregnancy and can cause significant maternal and neonatal adverse effects, including large-for-gestational-age infants, macrosomia, birth trauma, neonatal respiratory distress, and neonatal hypoglycemia.

Effective prevention and treatment strategies are essential to mitigate these risks. This systematic review aims to present and evaluate the current evidence on various interventions for preventing and managing GDM. The review will explore the effectiveness of dietary supplementation, lifestyle modifications, pharmacological treatments, and the use of probiotics. Additionally, the study will highlight the importance of accurate prevalence estimates and standardized diagnostic criteria in improving the allocation of health resources and the formulation of prevention and management policies.

Methodology

This systematic review was conducted by searching relevant studies related to gestational diabetes mellitus (GDM) on key databases such as PubMed, Medline, and Google Scholar. The literature search included, systematic reviews and meta-analyses published up to 2024. Inclusion criteria focused on studies that provided detailed information on the prevalence, prevention, and treatment of GDM. Data extraction and quality assessment were performed independently by multiple reviewers to ensure accuracy and consistency.

GDM and Diagnosis

Gestational diabetes (GDM) is a condition where high blood sugar levels are first identified during pregnancy. It's crucial to regulate blood sugar promptly to prevent complications during pregnancy. GDM is linked not only to perinatal complications but also to a higher risk of developing diabetes and cardiovascular disease in the mother later in life, as well as an increased chance of childhood obesity in the offspring [1,2,3]. While many women can manage this through lifestyle adjustments, such as dietary changes, some may require insulin injections or oral medications [4]. The pathophysiologic basis of GDM can be summarized as a relative insulin insufficiency. The placenta is responsible for supplying water and nutrients to the fetus, as well as producing various hormones to maintain the pregnancy [5]. During pregnancy, the placenta produces diabetogenic hormones such as human placental lactogen, which lead to insulin resistance, particularly in late pregnancy [6]. The contra-insulin effect occurs when certain hormones, such as cortisol, human placental lactogen, and estrogen, block the action of insulin. This effect typically begins around 20 to 24 weeks into pregnancy. In most cases, the pancreas can increase the amount of insulin it produces in response to insulin resistance [5]. Being overweight (body mass index [BMI] 25.0-29.9 kg/m²) or obese (BMI ≥30.0 kg/m²) is the most significant modifiable risk factor for GDM, with the risk being up to five times higher in morbidly obese women compared to women of normal weight. Other modifiable risk factors for GDM include unhealthy dietary habits, physical inactivity, and cigarette smoking. Additionally, the increasing average age at childbirth in Europe plays a significant role in the prevalence of GDM, as advanced maternal age is a well-known risk factor. The likelihood of developing GDM also increases with a previous history of GDM, macrosomia, excessive gestational weight gain, spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, neonatal hypoglycemia, hyperbilirubinemia, neonatal respiratory distress syndrome, family history of type 2 diabetes mellitus (T2DM), polycystic ovary syndrome, parity, and non-white ancestry [7].

GDA is the most frequent medical complications of pregnancies, affecting around 12-18% [8], which is associated with abnormal glucose tolerance that begins or is first recognized during pregnancy. This type of diabetes is usually diagnosed between 24 to 28 weeks of pregnancy. GDM can cause neonatal and maternal adverse effects such as large-for-gestational-age (LGA) infants, macrosomia, birth trauma, neonatal respiratory distress, neonatal hypoglycemia [9,12,13], cesarean section, preterm delivery, low Apgar scores, and an increased risk of cardiovascular disease or type 2 diabetes later in life [10].The most common

consequence of this type diabetes is macrosomia, which can lead to increased risk of shoulder dystocia and cesarean cut [11]. International Association of Diabetes in Pregnancy Study Groups (IADPSG) recommends using fasting plasma glucose (FPG) values of 5.1–6.9 mmol/L before 24 weeks of gestation and one-step 2-hour 75 g OGTT in the second trimester of pregnancy (between 24-28 weeks of gestation) to diagnose GDM [10].

Treatment

Comparison of Insulin Versus Metformin Treatment

Compared to insulin, metformin significantly reduces maternal outcomes such as preeclampsia, labor induction, and cesarean delivery, as well as neonatal outcomes including macrosomia, NICU admission, neonatal hypoglycemia, and being large for gestational age (LGA). However, it does not have a significant impact on maternal outcomes such as gestational hypertension, spontaneous vaginal delivery, and emergency cesarean section, nor on neonatal outcomes such as shoulder dystocia, premature birth, polyhydramnios, birth trauma, 5-minute Apgar score < 7, small for gestational age (SGA), respiratory distress syndrome (RDS), jaundice, and birth defects. The risk of having an SGA infant with metformin is similar to that with insulin. Furthermore, using metformin on its own decreases the likelihood of macrosomia, preeclampsia, and neonatal hypoglycemia when compared to insulin. These observations need to be validated with additional prospective studies and long-term follow-ups to better understand their enduring health impacts. There are advantages of using metformin instead of insulin such as oral administration, reduced hypoglycemic risk compared to insulin, and potential benefits in preventing the progression to type 2 diabetes postpartum [14, 15].

Immediate Versus Deferred Treatment

Another paper by Simmons et al. studied the treatment of GDM diagnosed before 20 weeks of pregnancy, comparing immediate treatment with deferred or no treatment. Immediate treatment led to a minor reduction in a composite of adverse neonatal outcomes, such as preterm birth, birth trauma, respiratory distress, phototherapy, stillbirth, neonatal death, or shoulder dystocia. There was no significant difference in pregnancy-related hypertension (preeclampsia, eclampsia, or gestational hypertension) between the immediate treatment and control groups. No significant difference in neonatal lean body mass was observed between the groups [17].

Early Benefits of Metformin Treatment

Dunne et al. compared the effects of early metformin treatment in women with GDM to insulin treatment. Early metformin intervention reduced maternal complications such as preeclampsia and labor induction needs compared to insulin. Additionally, the reduced weight gain observed in the metformin group is probably due to less insulin usage and metformin's direct impact on food intake. Metformin use was linked to fewer adverse neonatal outcomes: reduced rates of macrosomia, NICU admissions, neonatal hypoglycemia, and LGA cases. However, there was an increase in infants who were born weighing less than 2500 grams or classified as SGA. A reduction in crown-heel length was also observed in the metformin group, necessitating continued monitoring [15].

Precision Medicine in GDM Treatment

Benham et al. proposed a method which focuses on identifying specific markers to predict the effectiveness of lifestyle changes and medications for individual patients with GDM. This approach aims to tailor treatment more precisely based on markers like BMI, previous GDM history, family history of diabetes, HbA1c levels, and blood glucose levels at the oral glucose tolerance test (OGTT). Higher BMI and previous GDM history were strong indicators for the necessity of insulin therapy. Additional markers, such as maternal genetic profiles and lipid levels, also require wider investigation. Implementing these findings in clinical practice could optimize GDM treatment, improving maternal and neonatal outcomes, but further, more tailored studies are needed [4].

Combining Metformin with Insulin

Boggess et al. observed that combining metformin and insulin can reduce the probability of delivering a large for gestational age (LGA) baby. However, this finding needs further investigation to understand the underlying mechanisms and clinical implications [16].

Long-Term Benefits of Metformin

García-Patterson et al. reviewed medium to long-term outcomes and suggested that metformin might reduce the risk of developing type 2 diabetes post-pregnancy. The meta-

analysis indicated a significant reduction in the incidence of type 2 diabetes among women treated for GDM, with relative risk reductions ranging from 30% to 50% compared to untreated or poorly managed GDM cases [18].

Comparison of Metformin and Glyburide

Oliveira et al. showed that there are no differences in safety and efficiency between metformin and glyburide. Both drugs had similar effects on fasting and postprandial blood glucose levels and birth weight. However, metformin was associated with significantly less weight gain during pregnancy. Overall, treatment research on GDM suggests that metformin can be an effective drug option. It offers several advantages over insulin in reducing specific adverse effects. However, further research, including prospective studies and long-term follow-ups, is needed to validate these insights and understand their enduring health impacts [19].
Overall, treatment research on GDM suggest that metformin can be an effective drug option. It offers several advantages over insulin in reducing specific adverse effects. However, further research, including prospective studies and long-term follow-ups, is needed to validate these insights and understand their enduring health impacts.

Prevention

Gestational diabetes mellitus (GDM) is a significant health concern for pregnant women. Even though this disease is well-known, there still aren't many prevention strategies. In this research, we aim to present and review new strategies that are currently being studied, such as dietary supplementation, lifestyle modifications, and pharmacological treatments.

Dietary Supplementation with Myo-Inositol

There are many studies investigating the effectiveness of myo-inositol supplementation in preventing GDM among overweight and obese pregnant women. Motuhifonua et al. reviewed six randomized controlled trials (RCTs) with a total of 887 participants. It showed that taking 4 grams of myo-inositol daily might lower the rates of GDM, pregnancy-induced hypertension, and preterm birth. But the reliability of this evidence is low to very low due to significant risks of bias and imprecision in the studies reviewed. Notably, no significant adverse effects from myo-inositol supplementation were reported. The researchers highlight the need

for more high-quality RCTs to confirm these findings and inform clinical practice guidelines [20, 21].

Greff et al. conducted an analysis that included eight RCTs with a total of 1,795 participants. The study showed that myo-inositol supplementation significantly reduces the incidence of GDM by half compared to placebo. It also decreases fasting glucose levels, the need for insulin treatment, and the risks of preeclampsia, gestational hypertension, preterm birth, and neonatal hypoglycemia. The study recommends administering 2-4 grams of myo-inositol daily from the first trimester in high-risk pregnancies to prevent GDM and its related outcomes [22].

Lifestyle Interventions

Lim et al. suggest that lifestyle interventions during that time, along with treatments using metformin and myo-inositol/inositol, can reduce the risk of developing GDM. Other studies found that diet and physical activity interventions may provide a greater reduction in GDM risks in older women or women without a history of GDM or polycystic ovary syndrome (PCOS), whereas metformin may be more effective in older women, those with higher fasting blood glucose, or with PCOS. A combined lifestyle intervention including physical exercise, and a Mediterranean diet accompanied by motivation support may be considered the most effective way to prevent GDM among high-risk women during pregnancy [23, 24, 25, 26, 27].

Probiotics

Probiotics can be a safe and efficient way for GDM prevention and management. A meta-analysis by Tabatabaeizadeh evaluated the impact of probiotic yogurt on GDM, using data from four studies with 533 participants. The study showed a significant correlation between probiotic yogurt consumption and a reduced risk of GDM. Additionally, there was a significant decrease in fasting plasma glucose levels in the probiotic yogurt groups [28].

Effectiveness of Various Interventions

Wu et al. examined the effectiveness of different interventions diet, physical activity, combined diet and physical activity, and medication in preventing GDM and managing gestational weight gain (GWG) in overweight and obese pregnant women. Studies show that

diet, physical activity, combined diet and physical activity, and medication did not prevent GDM in overweight/obese women. Renewed efforts are hence needed to seek new and effective interventions and to prevent obesity prior to conception. In terms of GWG management, all interventions except medication were effective, with diet alone being the most successful. While these interventions did not significantly prevent GDM, the combined diet and PA approach was the best for reducing GDM risk and controlling GWG [14].

Prevalence Estimates

Precise estimates of GDM prevalence worldwide and regionally are essential for the effective development of prevention and management protocols to address the rising rates of GDM. The study by Wang et al., using criteria established by the International Association of Diabetes in Pregnancy Study Group (IADPSG), provides estimates through a comprehensive meta-analysis of 57 studies from various regions. The study shows the higher prevalence of GDM diagnosed using IADPSG criteria compared to other diagnostic methods, the greater identification of GDM cases through the universal oral glucose tolerance test (OGTT) compared to selective screening strategies, and the increased prevalence of GDM in women aged 30 years and older compared to those aged 25-30 years. The study also reveals that high-income countries have a higher standardized prevalence of GDM at 14.2% compared to low- and middle-income countries, which have 12.7% and 9.2%, respectively. Furthermore, there is a significant lack of data from many countries, with 152 countries not having data that met the inclusion criteria for this analysis. This highlights the need for standardized diagnostic criteria and screening strategies to obtain accurate and comparable prevalence estimates. The health implications of GDM are significant, as it is associated with increased risks of perinatal morbidity, future diabetes, cardiovascular disease in mothers, and obesity in offspring. Thus, accurate prevalence estimates are crucial for the effective assignment of health resources and the formulation of prevention and management policies [29].

References to SPORT:

Bennett G. et al. says that engaging in supervised physical activity helps reduce the risk of gestational diabetes mellitus (GDM) during pregnancy. It is advised that pregnant individuals aim for a minimum of 600 MET·min·wk-1 of physical activity in the first trimester to lower

their chances of developing GDM. Furthermore, maintaining a healthy pre-pregnancy BMI is essential for the effective prevention of GDM through exercise [30].

In Cremona, systematic reviews concluded that thrice-weekly exercise sessions, whether aerobic or strength training targeting major muscle groups, could improve glycaemic control. Women with a high body mass index (BMI) at risk of GDM would also benefit from such interventions; however, women with previous GDM pregnancies and a normal BMI do not seem to reduce their risk of GDM through exercise. Huang conducted meta-analyses involving 618 women, showing that aerobic exercise reduced fasting blood glucose, postprandial blood glucose, and HbA1C in patients with GDM compared to conventional treatment. On the other hand, Bgengski in his systematic review focused solely on the effect of exercise on fasting plasma glucose as the primary outcome. They concluded that there was no difference between exercise and physical activity counseling compared with standard care in fasting plasma glucose levels. Additionally, there was no difference in secondary outcomes such as macrosomia, preterm birth, cesarean section, gestational age at delivery, and birth weight [31].

Conclusion

This systematic review consolidates the current understanding and research on GDM, its prevalence, prevention, and treatment strategies, highlighting key findings and areas for future research. The findings underscore the need for more high-quality, inclusive research to substantiate the effectiveness of various interventions in preventing GDM and improving maternal and neonatal health outcomes. Accurate prevalence estimates are crucial for the effective assignment of health resources and the formulation of prevention and management policies.

Disclosure

Author's contribution

Conceptualization: Aleksandra Łakoma and Maciej Choiński; Methodology: Marcelina Teresa Marzec; Software: Aleksandra Wydra-Rojek; Check: Paulina Wasiewicz- Ciach and Katarzyna Kutyła; Formal analysis: Anna Marszałek and Piotr Kuczyński; Investigation:

Weronika Zofia Marzec and Wojciech Jan Mokot; Resources: Piotr Kuczyński; Data curation: Marcelina Teresa Marzec; Writing - rough preparation: Aleksandra Łakoma and Maciej Choiński; Writing - review and editing: Aleksandra Wydra-Rojek and Paulina Wasiewicz-Ciach; Visualization: Wojciech Jan Mokot; Supervision: Weronika Zofia Marzec; Project administration: Katarzyna Kutyła and Anna Marszałek; Receiving funding - no specific funding. All authors have read and agreed with the published version of the manuscript.

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