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RISK OF TYPE 2 DIABETES IN WOMEN WITH A HISTORY OF GESTATIONAL DIABETES: ASSOCIATED FACTORS, PREVENTION STRATEGIES AND CLINICAL INTERVENTIONS

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Abstract: Objective: To assess the risk of developing type 2 diabetes mellitus (T2DM) in women with a history of gestational diabetes mellitus (GDM), investigating associated factors such as time to development of the disease after childbirth, influence of clinical factors and effectiveness of preventive interventions through a systematic literature review. **Methodology:** This is a structured literature review based on the PVO strategy. The search was carried out in the PubMed/MEDLINE database, using the terms "type 2 diabetes mellitus" and "gestational diabetes", combined with the Boolean operators AND, OR and NOT. Eighteen articles were selected for detailed analysis. **Results:** Women with a history of GDM have a significantly higher risk of developing T2DM compared to those who did not have the condition during pregnancy. Identified risk factors include maternal age over 35, family history of DM2, and fasting glucose between 100-125 mg/dL. In addition, pre-pregnancy obesity and excessive weight gain during pregnancy increase the risk of progression to T2DM. Pharmacological and behavioral interventions have been investigated as effective strategies to prevent this progression. **Final considerations:** It is essential to implement an early and structured approach to optimize the treatment of GDM and reduce the risk of progression to T2DM. Pharmacological interventions should be further studied as adjuvant treatments, as well as effective strategies for adherence to postpartum screening, including the use of digital technologies and personalized health programs. Further studies are needed to strengthen this evidence and guide more effective clinical practices.

Keywords: Diabetes Mellitus 2, Women, Pregnancy, Gestational Diabetes Mellitus.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a metabolic condition that affects approximately one in six pregnancies globally, and is characterized by glucose intolerance first diagnosed during the gestational period (Eng *et al.*, 2024). This condition is associated with adverse outcomes for both mothers and newborns, including a significant risk of progression to type 2 diabetes mellitus (DM2) in the postpartum period. Women who have GDM are up to eight times more likely to develop DM2 throughout their lives compared to those who had normoglycemic pregnancies (O'Reilly *et al.*, 2020).

The progression of GDM to DM2 is more frequent in the first five years after pregnancy, with up to 70% of women developing the disease during this period (Walker, Flannery and Mackillop, 2020). The most commonly associated risk factors include advanced maternal age, high body mass index (BMI), family history of diabetes and the degree of hyperglycemia during pregnancy (Shin *et al.*, 2022). In addition, 25.9% of women who have had GDM progress to hyperglycemia as early as the first year after giving birth, according to Kindermann, Costa and Júnior (2022).

GDM is widely recognized as an independent risk factor for the development of DM2, and it is essential to understand the mechanisms that lead to the transition from one condition to the other. Although strategies such as lifestyle changes, weight control and glycemic monitoring show potential to mitigate risk, their long-term effectiveness is not yet well documented (You *et al.*, 2021). In addition, there is a lack of studies evaluating the impact of GDM treatment based on the updated 2013 World Health Organization (WHO) criteria, as many existing studies apply older criteria or include women without adequate treatment during pregnancy (Kgosidialwa *et al.*, 2024).

Although the risks are well established, adherence to screening for T2DM in the postpartum period among women with a history of GDM is low, ranging from 19.5% to 54%, even with clear recommendations from national and international protocols. In addition, the understanding of the pathophysiological factors underlying the transition from GDM to T2DM and the impact of preventive interventions in the postpartum period still require in-depth investigation (Evans *et al.*, 2021).

Factors such as obesity, insulin resistance and hypertension also need to be better investigated in populations with a history of GDM, considering their influence on both the development of DM2 and cardiovascular disease. These gaps are particularly evident in specific populations, such as Australia's First Nations, which have unique epidemiological characteristics (Madeira *et al.*, 2021).

Faced with these challenges, it is essential to develop more effective preventive and therapeutic strategies that not only reduce the incidence of DM2, but also improve the clinical outcomes of affected women. This study seeks to contribute to this area by assessing the risk of developing T2DM in women with a history of GDM, considering associated clinical factors, the time to progression to T2DM and the effectiveness of preventive interventions. In addition, the study aims to explore the pathophysiological mechanisms involved in the transition from GDM to T2DM, providing a basis for more effective follow-up and prevention strategies.

METHODOLOGY

This study is a literature review based on the PVO strategy, which considers the elements Population or research problem, Variables and Outcome. This strategy guided the formulation of the following research question: *"What is the risk of developing type 2 diabetes mellitus in women with a history of gestational diabetes, considering associated factors, time to progression and the effectiveness of preventive interventions?"*.

The searches were carried out in the PubMed/MEDLINE (Medical Literature Analysis and Retrieval System Online) database, using structured search terms combined with the Boolean operators "AND", "OR" and "NOT". The search strategy included the following terms: *("diabetes mellitus, type 2"[MeSH Terms] OR "type 2 diabetes mellitus"[All Fields]) AND "after"[All Fields] AND ("diabetes, gestational"[MeSH Terms] OR ("diabetes"[All Fields] AND "gestational"[All Fields]) OR "gestational diabetes"[All Fields] OR ("gestational"[All Fields] AND "diabetes"[All Fields] AND "mellitus"[All Fields]) OR "gestational diabetes mellitus"[All Fields])*.

The initial search identified 443 articles, which were subjected to strict inclusion and exclusion criteria to ensure the relevance and quality of the selected studies. The inclusion criteria included articles published in English between 2019 and 2024 that directly addressed the proposed topics. Review, meta-analysis, observational and experimental studies were included. On the other hand, the exclusion criteria eliminated duplicate articles, works available only as abstracts and studies that did not directly address the research question or that did not meet the other inclusion criteria.

After applying these criteria, 45 potentially eligible articles were identified.

Of these, 18 articles were selected to make up the body of evidence for this review. The included studies were analyzed in detail to assess the risk of developing T2DM in women with a history of GDM, considering associated factors such as obesity and family history. In addition, the time required for the progression of T2DM after childbirth and the effectiveness of preventive interventions, such as lifestyle changes and pharmacological therapies, were investigated.

This rigorous methodology aimed to ensure the quality and comprehensiveness of the review, allowing for an in-depth analysis of risk factors, the underlying pathophysiological mechanisms and the most effective strategies for preventing DM2 in women with a history of GDM.

DISCUSSION

RISK OF PROGRESSION FROM GDM TO DM2 AND ASSOCIATED FACTORS

Women with a history of GDM have a significantly higher risk of developing DM2 compared to those without this condition during pregnancy, with a higher risk observed up to four years after giving birth (Hu *et al.*, 2022). In addition, these women have a greater predisposition to developing comorbidities such as obesity, dyslipidemia, hypertension, metabolic syndrome and cardiovascular disease. Early detection of DM2 is crucial to avoid serious complications such as retinopathy, nephropathy, diabetic neuropathy, stroke and diabetic foot, which negatively impact quality of life (Nedergaard *et al.*, 2023).

The American Diabetes Association (ADA) recommends a glucose tolerance test (GTT) as an essential part of postpartum care for women with a history of gestational hyperglycemia, to be carried out between 4 and 12 weeks after delivery and repeated every 1 to 3 years, depending on individual risk (Hu *et al.*, 2022). Recent meta-analyses have confirmed that women with GDM have a seven times grea-

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ter risk of developing DM2. The International Diabetes Federation (IDF) reinforces the need for early interventions, such as lifestyle changes, to prevent metabolic complications and reduce health costs, especially in pregnant women at high risk of hyperglycemia (Wang *et al.*, 2024).

Observational studies and clinical trials have identified other risk factors for the development of DM2 after GDM, including maternal age over 35 years (a 5 to 6-fold increase), a family history of DM2 in first-degree relatives (a 2 to 3-fold increase in risk) and fasting glucose between 100-125 mg/dL (a 7-fold increase in risk). Lifestyle interventions, such as weight loss and increased physical activity, have been shown to be effective in preventing T2DM and can prevent the use of insulin and progression to inflammatory complications (Phelan *et al.*, 2021).

IMPACT OF LIFESTYLE AND DIETARY INTERVENTIONS

Evidence shows that lifestyle changes initiated after a pregnancy with GDM can reduce the risk of developing DM2 by up to 11%. Recent randomized clinical trials corroborate that intensive interventions, such as strict weight control and regular exercise, not only prevent obesity and cardiovascular problems, but also help to reduce glycated hemoglobin (HbA1c) levels in women who have already developed DM2 (Hu *et al.*, 2022).

Chen *et al.* (2021) found that women with pre-pregnancy overweight had a doubled risk of dysglycemia, while those with obesity had an almost tripled risk compared to women with normal weight. In the same study, women with GDM had a 12-fold increased risk of developing T2DM compared to those with no history of GDM, suggesting that effective weight loss strategies can substantially reduce this risk.

Hasbullah *et al.* (2023) reinforce the importance of nutritional interventions by demonstrating that dietary patterns rich in refined carbohydrates and confectionery are strongly associated with a greater likelihood of abnormal glucose tolerance (AGT) in post-GMD women. In addition, Wei *et al.* (2022) showed that pre-pregnancy obesity and excessive weight gain during pregnancy not only increase the risk of GDM recurrence, but also progression to DM2. The study highlighted high blood glucose values during the oral glucose tolerance test (OGTT), such as fasting blood glucose (5.43 ± 0.48 mmol/L), after 1 hour (10.93 ± 1.34 mmol/L) and after 2 hours (9.30 ± 1.66 mmol/L), as significant predictors of GDM recurrence ($p < 0.001$), emphasizing the need for constant monitoring.

PHARMACOLOGICAL INTERVENTIONS AND METHODOLOGICAL LIMITATIONS

Pharmacological interventions have also been explored as complementary strategies. Dennison *et al.* (2024), through a systematic review and meta-analysis, identified that metformin presents robust evidence in the prevention of DM2 in women with a history of GDM. The combination of metformin with sitagliptin showed superior effects in reducing glucose levels in consultations held 16 weeks after childbirth, while the use of these drugs alone had no significant impact. These results suggest that pharmacological intervention can play an important role in glycemic control, especially in women with additional risk factors.

However, the studies analyzed showed methodological variations and specific limitations. Chen *et al.* (2021), with a longitudinal cohort of 1,450 participants, demonstrated statistical robustness, but the geographical limitation restricts the generalization of the findings. On the other hand, Hasbullah *et al.* (2023), with a smaller sample of 157 post-GMD women, hi-

ghlighted the need to replicate the results in larger-scale studies. Wei *et al.* (2022), using data from 18 clinical centers in China with a significant sample of 6,204 women, acknowledged that the use of self-reports may have underestimated the real risk of DM2.

In addition, Ioannou *et al.* (2024) highlighted the effectiveness of interventions based on physical activity in 48 studies, although the lack of uniformity between interventions limited the comparability of results. Arab *et al.* (2023) found that only 56% of women had their blood glucose tested six weeks after giving birth, reinforcing the need for strategies to increase adherence to postpartum screening, such as the use of digital technologies and community health programs.

FINAL CONSIDERATIONS

Pregnant women with GDM have an eight times greater risk of developing T2DM in the postpartum period compared to normoglycemic pregnant women. Among the main risk factors are advanced maternal age, high BMI, family history of diabetes mellitus and hyperglycemia during pregnancy. Other factors, such as obesity, insulin resistance and hypertension, also seem to contribute to the development of T2DM, but require further studies to be properly clarified. Given this scenario, an early and continuous approach to screening for new cases of GDM and preventing progression to DM2 is essential. Effective strategies should include lifestyle changes, adherence to clinical treatment and further studies into pharmacological approaches in order to optimize maternal outcomes and reduce the risk of future metabolic complications.

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