

# The impact of pregnancy on diabetes

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## Summary

Gestational diabetes (GDM) impacts approximately 17 million pregnancies worldwide. Women with a history of GDM are at a significantly higher risk, around 8-10 times, of developing type 2 diabetes compared to those without prior GDM. Moreover, they face a twofold increased risk of developing cardiovascular disease (CVD). Despite the potential to prevent or delay the progression of GDM to type 2 diabetes, this approach is not widely implemented. With the increasing rates of type 2 diabetes and CVD among

women globally, it is essential to utilize the pregnancy period as an opportunity to identify individuals at risk and initiate preventive measures. This article critically evaluates the current clinical guidelines for identifying and managing women with previous GDM during the postpartum period. Additionally, it highlights important recommendations for preventing or delaying the progression to type 2 diabetes, with the aim of informing clinical practice worldwide.

**Keywords:** pregnancy, diabetes

## Introduction

It is estimated that there are currently approximately 537 million individuals worldwide living with diabetes, and this figure is expected to rise to over 643 million by the year 2030. Pregnancy induces various changes in both structure and function within the body, acting as a biological “stress test” for the maternal organ systems. Increasing evidence indicates that complications during pregnancy can signal and hasten maladaptive physiological changes in the mother, particularly in the cardiovascular and metabolic systems. One of the most prevalent complications during pregnancy is gestational diabetes mellitus (GDM), characterized by elevated blood sugar levels first detected during pregnancy and usually resolving shortly after childbirth.<sup>1,2</sup> Nevertheless, GDM still presents long-term risks. GDM affects around 13.4% (approximately 17.0 million) of pregnancies globally, placing both the mother and the infant at a heightened risk of developing type 2 diabetes and other health issues later in life. Women with a history of GDM face an 8-10 times higher risk of developing type 2 diabetes compared to those without such a history, with the greatest risk occurring 3-6 years after a GDM pregnancy. Moreover, a small percentage (0%-9.45%) of women with a history of GDM may develop type 1 diabetes postpartum. Additionally, women who fail to attend their postnatal follow-up appointments are also at an elevated risk of developing cardiovascular disease (CVD). A recent meta-analysis involving over 5 million women demonstrated that women with a history of GDM have double the risk of developing CVD compared to those without GDM.<sup>3,4</sup>

In comparison to women with gestational diabetes mellitus (GDM) who did not need insulin treatment, it is crucial to acknowledge that pregnancy presents a unique chance to detect potential adverse maternal health issues. This awareness enables better recognition, anticipation, early identification, and most importantly, the application of preventive measures. A well-defined pathway is essential to effectively handle women with a history of GDM in the initial postnatal period.<sup>5</sup> Various factors contribute to a faster progression to type 2 diabetes, such as hyperglycemia detected in the first trimester, the severity of glucose

intolerance and insulin needs during pregnancy, the gestational age at GDM diagnosis, excessive weight gain during pregnancy, the failure to shed pregnancy-induced weight gain after childbirth, a history of GDM in a prior pregnancy, and a shorter duration of breastfeeding. Moreover, prolonging the postpartum monitoring period to screen for type 2 diabetes enhances the detection rate, offering an opportunity for earlier intervention and prevention of long-term complications. Conversely, it is equally important to pinpoint women with GDM who may have a lower risk or specific requirements during pregnancy.<sup>6-10</sup>

## Results

Despite variations in the prevalence of hyperglycemia during pregnancy across different populations, there are specific clinical criteria that can help identify women who may need further evaluation to ensure optimal management of their condition and promote the optimal growth of the fetus. However, postpartum follow-up after gestational diabetes mellitus (GDM) remains limited in many parts of the world, despite clear evidence of the significant risks it poses to women after delivery. This limited follow-up can be attributed to various factors, including constraints within healthcare systems, personal barriers, and challenges faced by patients.<sup>11-15</sup>

After giving birth, many women experience emotional stress and anxiety as they navigate the challenges of motherhood. In such circumstances, attending postpartum testing, especially in a fasting state, becomes difficult for these women. Research indicates that even those who do return for postpartum follow-up often encounter a lack of continuity and inadequate care and coordination from the healthcare system. This is primarily due to time constraints in overwhelmed hospitals and insufficient communication regarding health risks and the importance of postpartum visits. Furthermore, there is limited consideration given to patients' understanding of the issue, which further contributes to suboptimal postnatal follow-up.<sup>16-20</sup>

The low uptake of postpartum screening is concerning as it may lead to missed opportunities for early intervention. In low- and middle-income countries (LMICs), postpartum screening is largely unavailable

due to weak healthcare systems, lack of awareness, difficulties in accessing healthcare, and limited availability of medications. Current recommendations for postpartum follow-up include a 2-hour oral glucose tolerance test (OGTT) at 6-12 weeks postpartum using the diabetes criteria applicable to nonpregnant women, a fasting glucose test at 6-13 weeks postpartum, or a glycated hemoglobin (HbA1c) test. The OGTT is currently considered the gold standard for detecting diabetes.<sup>21-24</sup>

Conducting the test mentioned is a time-consuming process that involves fasting and multiple blood draws, often resulting in reduced patient compliance. This is particularly challenging for nursing mothers who are caring for a newborn. Furthermore, the lengthy waiting times due to a high number of patients and the 2-hour duration of the test contribute to the inconvenience. For women residing in rural areas, the 2-hour oral glucose tolerance test (OGTT) becomes even more burdensome and impractical as they must travel long distances to access clinical healthcare. This guidance is intended for healthcare professionals who are involved in the care of women diagnosed with gestational diabetes mellitus (GDM) during and after pregnancy.<sup>25,26</sup>

Effective management of GDM necessitates a collaborative approach involving various professionals such as general practitioners, midwives, nurses, community health workers, dietitians, and nutritionists. These professionals play a vital role in delivering primary care, gynecological care, and support to women during and after pregnancy. Additionally, their respective professional organizations should also adhere to the noncommunicable disease (NCD) prevention guidance provided here. Healthcare delivery organizations and providers should also consider the resource needs of this specific population. The healthcare delivery system should take into account the World Health Organization's revised seven building blocks of the health system.<sup>27,28</sup>

Two distinct methods can be employed when evaluating the risk of women with gestational diabetes mellitus (GDM) progressing to type 2 diabetes. The initial approach entails identifying additional risk factors that are specific to the pregnancy complicated by GDM, which indicate a heightened likelihood of developing type 2 diabetes. On the other hand, the second approach involves assessing postpartum factors, either with or without considering factors that were present during pregnancy, such as impaired glucose tolerance (IGT), impaired fasting glucose, or other established risk factors for incident diabetes. Various examples of these contrasting approaches are discussed in this context. It is crucial to acknowledge that women who receive a diagnosis of hyperglycemia during early pregnancy are more prone to having pre-existing prediabetes or undiagnosed type 2 diabetes. Consequently, these women face an increased risk of developing type 2 diabetes after giving birth. This is particularly noteworthy in light of the current epidemic of childhood obesity and the prevalence of young-onset diabetes.<sup>29,30</sup>

### Body mass index

In the realm of diabetes research, there has been a recent focus on developing risk models to identify individuals who may be at a higher risk of developing type 2 diabetes. These models are designed to detect undiagnosed conditions or prioritize those who are more likely to progress towards diabetes, allowing for targeted lifestyle or behavior modifications.<sup>31</sup> While these models have proven to be cost-effective and applicable to the general population, there is a notable absence of risk stratification models specifically tailored for postpartum women or those with a history of gestational diabetes mellitus (GDM).<sup>32</sup>

Most prediction models currently in use incorporate major risk factors such as age, body mass index (BMI), waist circumference,

hypertension, family history of diabetes, and fasting glucose levels. However, only a limited number of models take into account important predictors specific to pregnancy, such as prior GDM, insulin use for GDM, gestational weight gain, and duration of breastfeeding. These factors hold particular relevance for women in the postpartum period and should be considered when developing risk models for this population.<sup>33</sup>

Moreover, there is a growing interest in the identification of biomarkers that can assist in the classification of the risk of developing type 2 diabetes in women with gestational diabetes mellitus (GDM). These biomarkers have the potential to improve the accuracy of risk assessment and enable targeted interventions for individuals at high risk.<sup>34</sup>

Genetic variations, epigenetic markers, and metabolomics have demonstrated promise as tools for risk stratification and the identification of women at high risk for specific conditions. However, their current limitations include suboptimal sensitivity and specificity, potential costs, and limited accessibility.

To effectively implement postpartum screening, a practical approach is necessary, incorporating simple risk scores or fasting glucose/HbA1c tests to facilitate acceptance and adherence. The testing for ongoing prediabetes and diabetes following a GDM pregnancy remains challenging due to the conflicting objectives of detecting all women at risk and the feasibility of implementing testing in routine clinical practice.<sup>35-37</sup>

Nevertheless, alternative protocols and less burdensome tests have been assessed to overcome the challenges associated with the oral glucose tolerance test (OGTT). For instance, a study conducted by Balaji et al.<sup>24</sup> summarized the recommendations provided by professional organizations, with some advocating for fasting glucose as the preferred option.<sup>38</sup>

Waters et al. evaluated the effectiveness of OGTT testing during the immediate postpartum period and the conventional 4-12 week time frame, discovering that while a normal early OGTT could essentially rule out overt type 2 diabetes at 4-12 weeks, its negative predictive value for diabetes or prediabetes combined was only 75%.<sup>39</sup>

### HbA1c

HbA1c is an appealing choice for postpartum testing because it does not require fasting. However, a systematic review discovered that its sensitivity in diagnosing diabetes in postpartum women with gestational diabetes mellitus (GDM) was only 36%, while its specificity was moderately high at 85%. Consequently, the review concluded that HbA1c was not a suitable test for postpartum diagnosis in this particular population. Similarly, fasting glucose evaluation was found to have a low sensitivity of 29% for diabetes. Nevertheless, when a combined approach involving both HbA1c and fasting glucose was utilized to determine the necessity of a formal oral glucose tolerance test (OGTT), it exhibited a high sensitivity of 82% and specificity of 92%, effectively reducing the burden of OGTT by 70%.<sup>40-43</sup>

Despite a similar report by,<sup>44</sup> the combination of HbA1c and fasting glucose has not been included in recent guidelines for postpartum testing. Furthermore, the rates of early postpartum testing following GDM are below 50% without specific follow-up and reminder programs. This can be attributed to a lack of clear responsibility for postpartum care within the healthcare system. The transfer of information regarding GDM diagnosis from obstetric/midwifery care to primary care is inadequate, resulting in a lack of necessary information for appropriate follow-up strategies.<sup>44-47</sup>

Therefore, it is imperative for policymakers and healthcare systems to prioritize systematic postpartum visits for all women with a history of GDM. The responsibility for postpartum follow-up bookings and reminders should be assigned to sectors within the healthcare system that are best equipped to handle this role. Additionally, a multifaceted strategy that focuses on developing capability, opportunity, and motivation should be implemented to enhance postpartum follow-up. It is also crucial to consider the purpose of follow-up after GDM.<sup>48</sup> (Figure1-4)

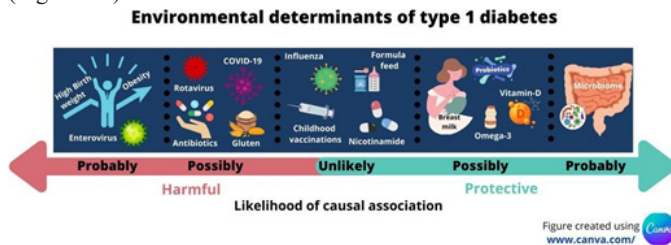


Figure 1 Environmental determinants of type 1 diabetes.

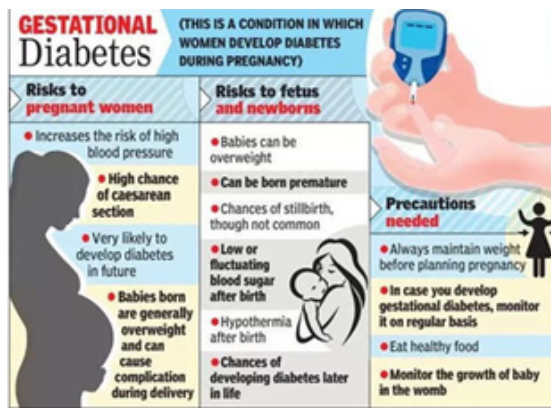


Figure 2 Gestational diabetes (women develop diabetes during pregnancy).

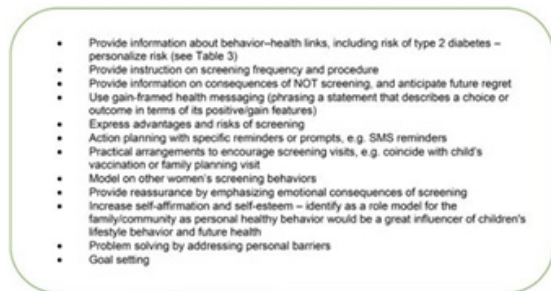


Figure 3 Information that should be imparted to women in order to foster behavioral change.

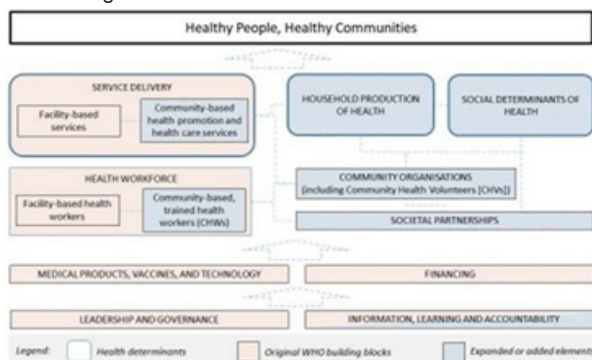


Figure 4 Current challenges and research priorities that can be addressed throughout a woman’s reproductive lifespan.

If the main goal is to evaluate the risk of developing diabetes during the immediate postpartum period, the oral glucose tolerance test (OGTT) may still be the most appropriate diagnostic test, despite its cumbersome nature. For women who have previously experienced gestational diabetes mellitus (GDM) and are planning to have another pregnancy, accurately diagnosing their glycemic status before conception can be considered beneficial. Incorporating postpartum testing into preconception care can help achieve this. In this particular scenario, accurately identifying impaired glucose tolerance (IGT) or type 2 diabetes is of clinical significance as it enables interventions to be implemented before pregnancy, thereby improving outcomes in subsequent pregnancies.

However, taking a life-course perspective, a diagnosis of GDM carries substantial long-term risks, such as the development of prediabetes, type 2 diabetes, and cardiovascular disease.<sup>44-50</sup>

**Individual-level approach**

Recommendations at the individual level have predominantly concentrated on enhancing knowledge and risk perception among women diagnosed with gestational diabetes mellitus (GDM). Nevertheless, there exists a dearth of recommendations that tackle personal obstacles faced by women, such as the apprehension of being diagnosed with diabetes, a lack of prioritization of personal well-being, and fatalistic attitudes. Conversely, personal facilitators encompass social support, a sense of reassurance following screening, and a family history of diabetes. Women with a family history of diabetes are more inclined to be concerned about developing the condition and are also more likely to adhere to lifestyle modifications aimed at preventing the disease. Consequently, interventions at the personal level must encompass a broad spectrum of modifiable factors. Figure 3 presents an overview of the information that should be imparted to women in order to foster behavioral change.<sup>49</sup>

**Lifestyle interventions**

Various populations have demonstrated success in reducing the risk of developing type 2 diabetes in women with a history of gestational diabetes mellitus (GDM) through lifestyle changes such as nutrition, physical activity, and weight management. This highlights the effectiveness of these interventions for women who have experienced GDM. Research has indicated that overweight women who followed personalized diet and exercise plans, maintained a food and activity diary, and attended group education sessions experienced more significant weight loss compared to those who received standard care. Therefore, when advising women on lifestyle modifications, it is crucial to offer guidance not only on what changes to make but also on how to successfully implement these changes.<sup>51</sup>

**Breastfeeding**

Moreover, breastfeeding is correlated with decreased blood glucose levels and a lower prevalence of type 2 diabetes in women who have experienced gestational diabetes mellitus (GDM) as well as in the general female population. Additionally, breastfeeding has been associated with postpartum weight reduction, a decreased long-term risk of obesity, and a lower occurrence of metabolic syndrome. Stuebe et al.’s research revealed a negative relationship between the duration of breastfeeding and the likelihood of developing type 2 diabetes in parous women participating in the Nurses’ Health Study I and II.<sup>52-54</sup>

In women who had given birth within the last 15 years, there was a notable 15% decrease in the risk of type 2 diabetes for each year of breastfeeding. This risk reduction persisted even after adjusting



for variables such as diabetes family history, dietary habits, physical exercise, and body mass index (BMI). These findings suggest that breastfeeding may have a significant impact on lowering the risk of type 2 diabetes in women, particularly those with a history of GDM.

To address concerns regarding the impact of exercise and diet on breastmilk quality, various studies have explored the growth patterns of breastfed infants whose mothers were attempting to shed excess weight. These studies indicated no significant alterations in the growth patterns of these infants in terms of weight or length, suggesting that a combination of breastfeeding, dietary modifications, and physical activity can be encouraged without compromising infant growth.<sup>55-56</sup>

It is crucial to highlight that women with a higher BMI might encounter difficulties in breastfeeding and might need extra assistance for lactation.

Furthermore, various randomized clinical trials have investigated the efficacy of pharmacologic interventions for preventing diabetes in women who have had gestational diabetes. Troglitazone and pioglitazone have demonstrated superior effectiveness compared to a placebo in preventing the development of type 2 diabetes. Nevertheless, it is advised against using these medications for women of childbearing age.<sup>57-60</sup>

## Pharmacological interventions

Conversely, females who disclosed a prior occurrence of GDM and took part in the Diabetes Prevention Program exhibited a noteworthy reaction to metformin treatment, leading to a substantial 50% decrease in the likelihood of developing diabetes. Nevertheless, for females without a previous self-reported history of GDM, the risk reduction associated with metformin was merely 14%. It is important to highlight that these medications are presently not endorsed for the prevention of diabetes, and additional research is required to assess their effectiveness and cost-effectiveness.<sup>61</sup>

## Surgical interventions

For appropriately selected obese patients, bariatric surgery can be an effective intervention to reverse glucose intolerance and type 2 diabetes, if it is available and deemed appropriate for the individual patient.<sup>62</sup>

## Population-level strategies

Policy-level factors are of utmost importance when it comes to tackling gestational diabetes mellitus (GDM) and its potential long-term effects. These factors encompass a range of elements, including the specific screening methods and criteria, well-coordinated reminder systems, and established protocols for documenting and sharing GDM history. Nevertheless, it is crucial to implement interventions at a population level to improve awareness and acceptance of the risk of developing type 2 diabetes among women who have previously experienced GDM.<sup>63</sup>

## Implementation

By enhancing awareness of potential risks, patients are empowered to make well-informed decisions regarding their health. Moreover, the discussion of management strategies post-diabetes diagnosis can offer patients reassurance and motivation to work towards achieving their screening objectives. Recognizing and addressing negative emotions can also play a pivotal role in encouraging a proactive attitude towards screening.<sup>64,65</sup>

Policies should be designed to enhance screening accessibility and accommodate lifestyle modifications. Overcoming obstacles such as

limited healthcare facility access and time constraints can facilitate increased post-pregnancy screening and care for women. Additionally, societal strategies should underscore the importance of women's health by emphasizing the significance of post-pregnancy screening and care. This involves striking a balance between motherhood responsibilities and self-care, while also addressing gender-based violence and mental health concerns through screening.<sup>66</sup>

## Opportunities for future follow-up and Intervention

Policy-level factors are essential in addressing gestational diabetes mellitus (GDM) and its potential long-term consequences. These factors include screening type and requirements, coordinated reminder systems, and protocols for documenting and communicating GDM history. However, interventions at the population level are crucial to raise awareness and acceptance of the risk of developing type 2 diabetes in women with a history of GDM.<sup>60-66</sup>

To achieve this goal, public education campaigns and online resources should be utilized to provide information about the susceptibility to type 2 diabetes, recommended screening frequency, the health implications of not undergoing screening, and the impact on future pregnancies. Increasing awareness of the risks can empower patients to make informed decisions about their health. Furthermore, discussing management strategies after a diabetes diagnosis can offer reassurance and motivate individuals to focus on achieving their screening goals. Acknowledging negative emotions can also play a role in promoting a proactive approach to screening.<sup>67-70</sup>

However, a personalized approach, such as making telephone calls instead of sending emails or letters, has been found to improve screening rates and enhance patient commitment. Research has also indicated that women participating in trials prefer receiving reminders via SMS over email, letters, or voice calls.<sup>70-72</sup>

To improve compliance rates and ensure that women with a history of gestational diabetes mellitus (GDM) do not have undetected diabetes in subsequent pregnancies, barriers and factors contributing to poor postpartum screening need to be addressed at both the individual and healthcare provider levels. The healthcare system can take several steps to address the issue of low postpartum follow-up rates and improve compliance.<sup>69-70</sup>

## Healthcare professionals

Healthcare professionals have identified two key challenges in communicating the diagnosis of GDM to pregnant women. The first challenge involves effectively conveying the risks associated with GDM while also providing reassurance. The second challenge is addressing immediate dangers to the infant without minimizing the future risks to the mother. The complexity of the messages related to GDM, combined with a clinical team that lacks a designated manager, leads to confusion among patients as they attempt to understand and navigate the condition. Each team member lacks the necessary knowledge and time to independently handle all aspects of patient care, yet there is no individual assigned to oversee or coordinate the care. This situation raises important questions about who should be responsible for arranging tests, when these tests should be scheduled, and who is accountable for issuing follow-up reminders or reporting results if the patient has been discharged before the scheduled test. Both healthcare providers and patients face constraints in terms of time and motivation to conduct or receive postpartum testing, which results in missed opportunities for continuous monitoring and prevention.<sup>66-70</sup>

Recent research, which compiled data from various systematic reviews, further reinforces the potential of mHealth interventions for

individuals with diabetes. The study concluded that these interventions offer a promising strategy for effectively managing diabetes and weight. Nevertheless, it is crucial to recognize that maintaining long-term engagement with these interventions poses certain challenges.<sup>66,67</sup>

It is important to highlight that preventive measures can have a lasting impact, even with a moderately intense intervention for up to a year post-childbirth. Such interventions have the capacity to delay or prevent the onset of type 2 diabetes. However, the implementation of these interventions in resource-limited settings may present obstacles.<sup>68</sup>

For example, a care model was trialed in a low-resource environment where women diagnosed with gestational diabetes mellitus (GDM) received continuous support throughout their pregnancy from trained healthcare providers. This model included in-person counseling sessions with nutritionists and healthcare professionals, educating women about GDM and its potential health risks for both mother and baby, distributing educational materials, and encouraging them to monitor their dietary habits and physical activity. The model demonstrated effectiveness in reducing the incidence of maternal and neonatal complications in women with GDM, comparable to those without the condition.<sup>69</sup>

Failing to address these concerns before the next pregnancy signifies a missed chance to improve the health of women and the outcomes of subsequent pregnancies. The International Federation of Gynecology and Obstetrics (FIGO) proposes extending preconception care into the postpartum stage to broaden the window of opportunity and reach women with additional needs, thereby offering a comprehensive continuum of care. There are six main themes that influence postpartum behavior and require further investigation:

- The role of motherhood and priorities,
- Social support,
- Life demands,
- Personal preferences and experiences,
- Risk perception and information and
- Financial resources (including the preferred format of interventions).<sup>73</sup>

These factors have hindered many women from addressing their own health, while motivating others to persist. Improving adherence to postpartum follow-up can be achieved by integrating diabetes screening with child vaccination programs or family planning visits, as well as utilizing mobile health (mHealth) and virtual visits. The prevalence of both gestational diabetes mellitus (GDM) and type 2 diabetes is increasing. If a woman is diagnosed with GDM, she is considered to have an elevated risk of developing type 2 diabetes. However, the effectiveness and duration of preventive measures for these women have not been optimized. Future research should focus on the following areas: enhancing preconceptional and interpregnancy care, improving maternal nutrition and reducing obesity, identifying new biomarkers and cost-effective tests for diabetes, and evaluating the implementation and impact of recommendations in real-world settings. Figure 4 provides an overview of the current challenges and research priorities that can be addressed throughout a woman's reproductive lifespan.<sup>70-74</sup>

## Acknowledgments

None.

## Conflicts of interest

Authors declare that there is no conflict of interest.

## Source of funding

None.

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