

Strategies to prevent Type 2 Diabetes in the postnatal period in women with history of Gestational Diabetes

Bolou Angeliki^{1,*} and Gourounti Kleanthi²

¹ School of Health Sciences, Institute for Lifecourse Development: Centre for Chronic Illness and Ageing, Faculty of Education, Health & Human Sciences, University of Greenwich, London, UK.

² Department of Midwifery, University of West Attica, Athens, Greece.

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Abstract

This literature review emphasizes the critical need for focused interventions to prevent Type 2 Diabetes (T2D) in the postnatal period, particularly for women with a history of Gestational Diabetes Mellitus (GDM). GDM poses a substantial risk, increasing the likelihood of T2D development by 11-fold later in life. With 14% of pregnancies worldwide affected by GDM, the escalating global T2D rates underscore the urgency for targeted postnatal strategies. Current interventions, such as those modelled after the Diabetes Prevention Program (DPP) and the Mediterranean Diet, show promise in reducing T2D risk by over 50%, yet challenges like low engagement persist. To address these complexities, future research should prioritize developing acceptable postnatal interventions, incorporating peer support, addressing barriers, and employing randomized controlled trials with larger participant cohorts. The multidimensional approach involves lifestyle modifications, dietary changes, behaviour change strategies, and exploration of pharmacological options, collectively contributing to a substantial reduction in the long-term T2D risk for women with a history of GDM.

Keywords: Diabetes; Gestational Diabetes; Prevention; Lifestyle Interventions; Pharmacological Interventions

1. Introduction

1.1. Prevention of Type 2 Diabetes in postnatal period

Gestational diabetes Mellitus (GDM) is the most common complication in pregnancy, with 14% of all pregnancies affected by GDM, worldwide.⁽¹⁾ GDM causes an 11-fold increase in the woman's risk of developing type 2 diabetes (T2D) later on in life.⁽²⁾ The global increase of T2D has led to the need for postnatal interventions for women with GDM.⁽³⁾ The lack of routine care for diabetes prevention in the crucial postnatal period has been identified and many different studies have tried to evaluate the best method to prevent diabetes and keep women engaged with the intervention in the long run.⁽⁴⁾ So far, interventions implemented in women at risk of developing T2D have focused on increasing physical activity, changing diet, using pharmacological treatments, adopting behaviour modification strategies and using goal-setting techniques, to reduce weight and promote a healthy lifestyle.⁽⁵⁻⁷⁾ These interventions have been found to reduce the risk of diabetes by more than 50% and have the potential to be beneficial for women with a history of GDM.^(4, 6, 7) However, some of the studies that focused on preventing the progression of GDM to T2D, recruited participants with a history of GDM, later on in life and not in the immediate postnatal period, delivered a short-term intervention, focused on weight reduction and not on diabetes or faced barriers with recruitment and were underpowered.^(4, 8, 9) It is evident, based on what was previously discussed, that development of effective postpartum interventions is necessary⁽²⁾ with the realistic potential to improve outcomes.

* Corresponding author: Bolou Angeliki

Since the risk is known, an opportunity arises in the postnatal period where women can be educated about diabetes prevention. This can potentially allow them to change their lifestyle, not only to prevent diabetes development but also to enter safely a subsequent pregnancy, as they would have received postnatal testing, extra follow-up appointments and preconception support.

1.2. Lifestyle interventions

Most studies in the postnatal period, for women with a history of GDM are implementing lifestyle interventions in an effort to reduce their diabetic risk. These interventions either introduce dietary changes and/or aim to increase physical activity. Fewer studies are focused on increasing awareness about the benefits of breastfeeding in lowering the risk of developing diabetes.⁽⁴⁾

The intervention that has been used as a pillar for the development of most postnatal studies, is the Diabetes Prevention Program (DPP), which was conducted in United States. This study included 350 women with previous history of GDM.^(10, 11) The DPP study randomised subjects to receive metformin or placebo, routine care or intense lifestyle intervention. In the past, the effectiveness of a lifestyle intervention versus metformin has been debated in regard to diabetes prevention, with both reported as beneficial, as they have successfully reduced the incidence of T2D in patients at risk, with lifestyle intervention proven to be even more effective.^(11, 12) However, for women with a history of GDM, both metformin and lifestyle intervention are equally highly effective and achieved a reduction of diabetes incidence by approximately 50% compared to the placebo group.⁽¹⁰⁾

The DPP study introduced an intense lifestyle intervention, and the two primary goals were a minimum weight loss of 7% and a minimum physical activity of 150 minutes a week. It implemented behaviour change methods to promote such an intense lifestyle change by utilising sixteen sessions tailored to teach coping and self-management strategies for physical activity and weight loss, used goal-setting features, gave access to lifestyle coaches, reinforced regular contact for participants in order to create a supportive environment and it tailored material to be ethnically diverse.⁽¹¹⁾ The diet goals were focused on fat reduction, increasing calorie load awareness and restricting portion sizes.⁽¹¹⁾ Women with GDM history were less able to maintain the specific level of activity and had a lower peak of weight loss compared to women without GDM history, despite this, over a three-year period, lifestyle change was still an effective treatment for diabetes prevention.⁽¹⁰⁾

The limitation of the DPP study is that it did not recruit women in the postnatal period and there is a loss of possible candidates due to T2D development, since the participants received their GDM diagnosis around 12 years prior to the study.⁽¹⁰⁾ A study group in Australia implemented the DPP lifestyle modification programme in women in the postnatal period with a history of GDM, three months after delivery and for the first postnatal year. This study is called MAGDA (Mothers After Gestational Diabetes in Australia). They demonstrated a 1 kg reduction in weight, which could reduce the woman's diabetic risk, but they faced the issue of low engagement.⁽¹³⁾ This leads to the conclusion that the effectiveness of an intensive lifestyle intervention in the first postnatal months has not yet been measured or proven to be achievable and acceptable. A systematic review suggests the initiation of the intervention as early as 6 weeks postnatally, as women are more prone to make lifestyle changes in the very early postnatal period.⁽⁴⁾ The reasons behind this, could be the fact that women might perceive their diabetic risk as being high right after pregnancy or because they are used to a high number of appointments and monitoring their glucose levels daily in pregnancy, which could lead to them being highly motivated to facilitate a change.

Several systematic reviews have shown that dietary and lifestyle interventions can reduce the risk of diabetes in women with GDM history, but most studies are pilot or feasibility studies and have not yet proven the effectiveness of the methods used.^(8, 14) Small RCTs with 20 to 40 participants have shown that physical activity can be increased in this population but not to the recommended level.⁽¹⁵⁾ Future interventions should adjust physical activity time, recommend walking as an activity or consider providing dietary interventions.⁽¹⁶⁾ A recent systematic review and meta-analysis looked at thirteen RCTs on lifestyle interventions compared to routine care, confirmed that lifestyle interventions can reduce T2D risk in women with GDM history. In addition, they also noted that the studies that were included had different follow-up periods varying from 4 to 36 months and the sample sizes were small (over half of the studies included were conducted in China).⁽¹⁷⁾ The studies vary at the timing that the intervention was introduced, from 2 months postpartum up to 14 years.⁽¹⁸⁾

There is an issue in the postnatal period with women receiving vague lifestyle suggestions from clinicians and not being aware of their risk of diabetes.⁽⁸⁾ A prospective cohort study has shown that women with a history of GDM frequently have low adherence to lifestyle interventions due to lack of social support.⁽¹⁹⁾

Future studies should take the element of peer-support into account, adopt a randomised controlled trial design with the involvement of more participants and introduce interventions in the first postnatal year. Taking into consideration the several questions that arise regarding acceptability and effectiveness of the aforementioned interventions to prevent diabetes, this results in a need for acceptable postnatal interventions that take into account the several barriers that are part of a busy postpartum schedule.

1.3. The Mediterranean Diet for Type 2 Diabetes Prevention

Apart from reducing fat and calorie intake, another diet that has been suggested for its usefulness in women with prior GDM is the Mediterranean Diet. The Mediterranean Diet is associated with lowered risk of gestational diabetes and improved glucose tolerance during pregnancy.^(20, 21) In addition, it can reduce cardiovascular risk by 52% in high-risk groups and reduce T2D risk by 20%.^(22, 23) A Mediterranean Diet is based on specific principles such as increased daily consumption of vegetables, whole grains, legumes, nuts and seeds, daily consumption of fresh fruit and extra-virgin olive oil (EVOO), low to moderate consumption of dairy products, poultry, eggs and fish and low consumption of red meat.⁽²⁴⁾

There is a study that assessed the effectiveness of Mediterranean Diet food habits in lowering the diabetic risk of women with GDM history. The Nurses' Health Study II (NHS II) showed that adherence to a healthful dietary pattern is linked to T2D risk reduction.⁽²⁵⁾ This study included the largest sample of participants which is 4,413 women and followed them for the longest period which is 16 years. It had several limitations such as that participants were mainly Caucasian and nurses which means that they possessed some knowledge regarding a healthy lifestyle. The acceptability of the diet to multi-ethnic groups is not known and the same applies for participants with different educational backgrounds. Another limitation is that participants were not introduced to the Mediterranean Diet, instead their dietary habits were assessed with specific validated food frequency questionnaires.⁽²⁵⁾ Women with history of GDM were part of the NHS-II but it is unclear in which point following GDM diagnosis. This study had a prospective design and initially measured outcomes focused on the use of contraceptive methods but later it expanded to investigating cancer, metabolic disorders and over 30 diseases.

A randomised controlled trial (RCT) that commenced the intervention 6 to 12 weeks postnatally showed that significantly fewer women with GDM history developed glucose disorders 3 years after following a Mediterranean diet and a monitored physical activity programme.⁽²⁶⁾ The study population was mainly Caucasian and Hispanic women (N=237), who might be more accustomed to this diet compared to a more ethnically diverse group. The Mediterranean diet might be effective in this population but the acceptability of the diet to different ethnicities has not been assessed yet. A recent pilot study introduced the Mediterranean diet in the postnatal period in a multiethnic population, but has not published the results yet.⁽²⁷⁾

1.4. Behaviour change theories

Lifestyle interventions should be underpinned by behaviour change theories as the effectiveness of an intervention can be enhanced by supporting participants to stay motivated and sustain behaviour change. The individual's health related behaviours should be considered at the developmental stages of the study. These behaviours can focus on investigating enablers, motivators, beliefs, attitudes, and difficulties that might affect participant's engagement with the study.⁽²⁸⁾ Coping strategies can be put in place in order to support and reinforce specific behaviours that would increase adherence and engagement. One model that can be useful for women with history of GDM in postnatal period for diabetes prevention is the COM-B model (Capability, Opportunity, Motivation and Behaviour)⁽²⁹⁾. Capability can increase by increasing knowledge about diabetes and supporting women to increase their confidence to follow a lifestyle intervention.⁽²⁸⁾ Opportunity is linked to personal barriers (for example childcare demands or lack of time) and how a supportive environment can be created to enable behaviour change, support can be provided by healthcare professionals, peers or from family members.⁽³⁰⁾ A known motivator for women with GDM history is the fear of type 2 diabetes development but the enabler is the woman's own confidence (self-belief) in being able to change.⁽²⁸⁾ Lifestyle interventions should provide participants with the opportunity to engage with other participants, consider how the intervention can be made culturally appropriate and educate participants about managing personal barriers.

1.5. Pharmacological interventions to prevent diabetes development

Several pharmacological interventions have been used for diabetes prevention in high-risk populations. The most common drugs used, for women with a history of GDM, are troglitazone, pioglitazone, metformin and dapagliflozin with metformin or alone.^(31, 32) Pharmacological studies in this population are limited, and some of them were underpowered or conducted several years following a GDM diagnosis.

Troglitazone has been used in the TRIPOD randomised controlled study in women of Mexican, Guatemalan or Salvadoran descent that had a 70% risk of developing T2D.⁽³³⁾ Breastfeeding women were excluded from the study. Troglitazone was used to improve insulin sensitivity and was found to be effective in the pilot trial that the study group conducted. Women received the intervention within 4 years after a GDM diagnosis and the length of the trial was meant to be 42 months.⁽³³⁾ The trial was terminated 4 months early as troglitazone was removed from the market due to hepatotoxicity.⁽⁸⁾ The study results were inconclusive and troglitazone was deemed as unsafe. The same study group invited participants without diabetes to receive pioglitazone, this drug was shown in the study to have an insulin-sensitizing effect but this was a small trial with only 64 participants completing the end of study follow-up at 3 years.⁽³⁴⁾

Metformin, an oral glucose lowering agent, was used in the DPP study, which included the largest sample size, compared to other pharmacological studies, looking at diabetes. A total of 350 women with history of GDM were recruited, the study showed a 50% reduction in diabetes development and metformin was found to be more effective in this group compared to women without GDM history. Participants received the intervention for 3 years when these study results were published, which in comparison with other studies is considered a long follow-up period.^(10, 35) Participants had a 12-year gap since their last pregnancy and considering that T2D development has the highest conversion rate in the first 5 years after delivery, many possible participants were lost due to the fact that they would already have a T2D diagnosis. The DPP study had comparable results to troglitazone which at the time showed a 55% risk reduction. Troglitazone was later discontinued, leading to metformin being the only safe drug that showed 50.4% risk reduction.⁽³⁵⁾ The safety and acceptability of the drug cannot be expanded to women of reproductive age, as women who were breastfeeding, women who were planning a pregnancy or women who did not take contraceptive measures were excluded from the study.⁽³¹⁾ A recent randomised controlled double-blind pilot study introduced metformin in the postnatal period for 1 year and included women who were breastfeeding and had normal glucose levels after the delivery, this study successfully recruited participants but was unpredictably affected by COVID-19 pandemic, which had an impact on adherence and engagement, with half of the participants adhering to metformin at the end of the study.⁽³⁶⁾

Dapagliflozin is a sodium-glucose co-transporter-2 (SGLT-2) inhibitor, which improves glycaemic control and promotes weight reduction.⁽³⁷⁾ A recent randomised trial looked at the effectiveness of dapagliflozin and metformin, alone and combined, on weight management in women with GDM history. The trial found that dapagliflozin with metformin had a greater positive effect on anthropometric and metabolic parameters.⁽³²⁾ The study recruited obese women (body mass index above 25) with a history of GDM in the past 12 months. The results were promising but should be interpreted with caution as only 49 participants completed the study, it lasted for only 6 months and started 6 weeks postpartum. Another limitation is that women should not be breastfeeding and should be using contraception in order to receive the study treatment, which means many women would be excluded.⁽³²⁾ The World Health Organisation (WHO)⁽³⁸⁾ advises women to exclusively breastfeed their infants for the first 6 months postnatally. By restricting the sample to women who do not breastfeed, the number of participants will be significantly reduced, since the intervention commences at 6 weeks postpartum. In addition, the participants are of reproductive age and might be planning another pregnancy and are at risk of an unplanned pregnancy. These restrictions justify the small sample of participants that completed the study.

In women of reproductive age, metformin is considered a safe drug to use during pregnancy and in the breastfeeding period.^(39, 40) The use of SGLT-2 inhibitors, including dapagliflozin, in pregnancy and in the breastfeeding period is not recommended.^(39, 41) Future studies in this field should focus on assessing the acceptability and effectiveness of metformin in the immediate postnatal period, as metformin is a safe drug to use and potentially can reduce diabetes risk in the early postpartum period. Based on the evidence discussed in this section there is a notable gap in research in pharmacological treatment in the first years after a GDM pregnancy.

2. Conclusion

The prevention of Type 2 Diabetes in the postnatal period, for women with a history of Gestational Diabetes Mellitus (GDM), is a crucial area that requires focused attention and effective interventions. The global rise in type 2 diabetes necessitates targeted postnatal interventions to mitigate this risk. Lifestyle interventions have shown promise in reducing the risk of T2D by more than 50%. However, challenges persist, including low engagement, difficulties in maintaining specific activity levels, and the need for interventions to commence in the early postnatal period. Pharmacological interventions, such as metformin, have demonstrated significant risk reduction in T2D development. Future studies should prioritize the development of acceptable postnatal interventions, safe for breastfeeding women, addressing barriers, incorporating peer support, and adopting randomized controlled trial designs with larger participant cohorts.

In conclusion, the prevention of T2D in the postnatal period requires a comprehensive and multidimensional approach, encompassing lifestyle interventions, dietary modifications, behaviour change strategies, and the exploration of pharmacological options. A concerted effort to develop and implement effective interventions during the critical postnatal period can significantly contribute to reducing the long-term risk of T2D in women with a history of GDM.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest

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