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Advances in the use of technology for the management of diabetes in pregnancy: a comprehensive review

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The increasing prevalence of diabetes in pregnancy worldwide, with the number of women with type 1 (T1D) or type 2 diabetes (T2D) or gestational diabetes mellitus (GDM) doubling over the past few decades, is a major challenge for clinicians [Mackin 2018, Feig 2014]. Pregnant women with poor glycaemic control face an increased risk of perinatal complications such as pre-eclampsia, preterm birth (delivery before 37 weeks gestation) and neonatal morbidity, including congenital anomalies, large for gestational age (LGA) birthweight (>90th percentile), increased rates of caesarean section, neonatal hypoglycaemia and neonatal intensive care unit admissions [McLean 2024, Murphy 2021].
The burden of these concerns is additionally aggravated for the affected women by the required efforts for a strict glycaemic control during pregnancy. Insulin sensitivity and absorption vary throughout gestation, making it difficult to maintain tight glycaemic targets while avoiding hypoglycaemic events in women [Garcia-Patterson 2010]. In recent years, advances in diabetes technology offer new opportunities by providing more accurate monitoring of glucose levels and more appropriate treatment optimisation.

In this review, we summarise the latest evidence on the use of CGM or HCL insulin pump therapy in pregnant women with type 1 or type 2 diabetes or GDM, and discuss challenges and considerations related to their applicability.

Continuous Glucose Monitoring (CGM) in Pregnancy

CGM systems measure interstitial glucose levels continuously and provide real-time data on glycaemic excursions, enabling more precise and timely adjustments in insulin therapy compared to traditional self-monitoring of blood glucose (SMBG) [Edelman 2018]. During pregnancy, variations in insulin sensitivity challenge women with diabetes, confronting them with a higher risk of hypoglycaemia in early pregnancy when insulin sensitivity increases during the first 16 weeks, following a sharp increase in insulin requirements from 16 to 37 weeks, and variable daily insulin absorption in late pregnancy [Garcia-Patterson 2010]. Even with early CGM devices, it was shown that pregnant women who used CGM in addition to capillary blood glucose monitoring had lower HbA_{1c} in late pregnancy, despite their then manifold limitations (limited accuracy, masked, not compatible with smartphones, no out-of-range alarms, uncomfortable size) [Murphy 2008, Murphy 2024]. Actually, the accuracy of the CGM device used becomes particularly important as the glycaemic targets during pregnancy are more stringent (HbA_{1c} optimally <6.5 % for the 1st trimester, HbA_{1c} <6.0 % in the second and third trimesters) and much narrower with a targeted time in range (%TIR 63 -140 mg/dL) of >70 % at least in women with type 1 diabetes [ElSayed 2023, Battelino 2019].

Several studies have collected evidence to support the benefits of CGM during pregnancy, but most of them included populations with type 1 diabetes. In the largest randomized controlled trial, the pivotal CONCEPTT (Continuous Glucose Monitoring in Women With Type 1 Diabetes in Pregnancy) study, continuous CGM use significantly improved glycaemic control in pregnant women with T1D from early pregnancy through to delivery. The study showed that women using CGM spent more time within the pregnancy-specific glucose target range and had lower HbA_{1c} levels compared to women applying SMBG. Significant reductions in the risk of LGA infants, neonatal hypoglycaemia and neonatal intensive care unit admission were associated with the improvements in glycaemic control [Feig 2017].

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Achieving a higher time in range (TIR) was associated with better neonatal outcomes in further analysis of the CONCEPTT trial. Specifically, each 5-7 % increase in TIR during the second and third trimesters was associated with a reduced risk of neonatal hypoglycaemia [Yamamoto 2019].

In a real-world cohort study of a Swedish population of 186 pregnant women with T1D using CGM, a high percentage of time in target in the second and the third trimester was associated with lower risk of LGA [Kristensen 2019]. Subsequent studies have supported these findings by showing, for example, that each 5 % increase in TIR was associated with a reduction in the risk of pre-eclampsia by 45 % and of LGA by 46 % in women with T1D [Sobhani 2024], respectively, and a 28 % reduction in the odds of neonatal morbidity in pregnancies with pre-existing T1D or T2D [Sanusi 2024]. These studies underline the importance of maintaining a high TIR during pregnancy in order to optimise both maternal and neonatal outcomes.

Currently, the evidence to fully support the use of CGM in pregnancies with type 2 diabetes or GDM is limited. The available relevant studies have used CGM data more as a tool for structured education, through the use of blinded devices and/or short-term use [Yoo 2023, Alfadhli 2016, Paramasivam 2018, Yu 2014]. One recent study showed a benefit of intermittently scanned CGM (is-CGM) on fasting and postprandial glucose levels as well as risk of fetal macrosomia in women with GDM using the device intermittently in the first 4 weeks after GDM diagnosis compared with the control group using SMBG [Majewska 2023].

CGM use can indeed provide valuable feedback and support optimal self-management of diet and physical activity, even when used intermittently in T2D or GDM affected pregnancies. Some guidelines suggest that CGM should be considered in those receiving insulin therapy [Yoo 2023, Diabetes in pregnancy 2020].

In this context, randomised clinical trials are underway to assess the effects of CGM (Dexcom G6) in 40 pregnant women with type 2 diabetes (Adopting technology for glucose optimization and life-style in pregnancy [AT GOAL] study, NCT05370612) and in a larger sample of > 372 pregnancies with GDM (The Effectiveness of Rt-CGM to Improve Glycemic Control and Pregnancy Outcome in Patients With GDM, NCT03981328) [Huhn 2020].

Hybrid Closed-Loop (HCL) Systems in Pregnancy

The newly introduced HCL systems combine CGM readings with an insulin pump to create a feedback loop via a mathematical control algorithm that automatically adjusts insulin delivery based on real-time glucose readings. However, manual input is still required to alert the system when eating or exercising. This automation helps to reduce the burden of diabetes management and achieve tighter glycaemic control in children, adolescents and adults with T1D [Boughton 2021]. Thus, HCL systems were thought to adapt better to physiological changes during pregnancy, including increased insulin resistance and altered insulin pharmacokinetics.

The Automated Insulin Delivery Amongst Pregnant women with Type 1 diabetes (AiDAPT) trial is a landmark study evaluating the efficacy of the CamAPS FX HCL system during pregnancy. The study found that women using the HCL system had significantly higher TIR compared to women using standard insulin therapy with CGM spending 10.5 % more in TIR from 16 weeks' gestation until delivery. The benefits of HCL use were evident as early as the first trimester and continued to increase throughout pregnancy. Women using the HCL system also experienced less gestational weight gain and reported improved quality of life, with less anxiety associated with glucose management [Lee 2023].

The outcomes from CRISTAL, another randomised, controlled, parallel-group study comparing Medtronic's 780G HCL system with standard insulin therapy in pregnant women with T1D, were less encouraging. The results showed no significant difference in TIR between the HCL and standard insulin therapy groups (66.5 % vs. 63.2 %), with no improvement in mean glucose or reduction in hyperglycaemic metrics throughout pregnancy. There were small benefits in terms of overnight glucose control and treatment satisfaction, and a reduction in the rate of hypoglycaemic events. The recommended pregnancy-specific TIR of 70 % was not achieved until 33 to 36 weeks' gestation [Benhalima 2024].

The different results can be explained by a closer look at the two systems: The CamAPS FX system uses an adaptive algorithm (adjustment over 24 h, after meals and daily), allows lower glucose targets and takes into account weight changes. The algorithm of the Medtronic 780G system is less adaptive and requires additional user input, such as fake carbohydrates, to compensate for hyperglycaemic (mainly postprandial) excursions [McLean 2024]. Additionally, looking at real-world data, in a multicentre cohort from Spain, off-label use of com-

ABSTRACT

Pregnancies affected by any form of diabetes whether those with pre-existing type 1 or type 2 diabetes or those who develop gestational diabetes during second or third trimester are subjected to an increased risk of adverse pregnancy outcomes. Improved glycaemic control before and throughout pregnancy as well as postpartum may substantially reduce the risk for adverse complications, but this is very difficult to achieve. Recent advancements in diabetes technology, including continuous glucose monitoring (CGM) and hybrid closed-loop (HCL) insulin delivery systems, are candidates to transform the management of diabetes in pregnancy by ameliorating glycaemic control, reducing the incidence of unfavourable consequences, and improving the quality of life for pregnant women with diabetes. This review focuses on the current evidence evaluating the effectiveness of these technologies during pregnancy and their impact on maternal and neonatal outcomes.

mercially available HCL systems, mostly the Medtronic 780G system, not only failed to improve glycaemic control, but also resulted in higher total daily insulin doses, greater gestational weight gain, and higher birth weight compared to controls receiving multiple daily injections [Quirós 2024]. Therefore, from the available data, we can conclude that in pregnancy it is important to consider system-specific features before offering available HCL technology to ensure clinical benefit and pregnancy outcome.

Challenges and Considerations

In addition the debate about the clinical benefits of advanced technologies in pregnancy, there are other challenges to consider. Access to these technologies is one of the main challenges. CGM and HCL systems are expensive and their prescription is often limited by health insurance coverage conditions. This can lead to disparities in care for women from lower socioeconomic backgrounds.

Another neglected aspect are the efforts and need for education and support for both users and healthcare providers. Effective and accurate use of CGM and HCL systems require a solid understanding of how these technologies work and how to interpret and manage the vast amount of data they provide. This requires an ongoing training capability, which can be a resource-intensive process for both healthcare providers and patients.

More research is also needed to establish more detailed and accurate evidence-based guidelines for the use of CGM and HCL systems during pregnancy. There are still many unanswered questions, particularly regarding the optimal targets for CGM metrics for all types of diabetes and the best practices for integrating these technologies into clinical care.

Conclusion

The integration of CGM and HCL systems into the management of diabetes during pregnancy can significantly advance maternal and neonatal care. These technologies may improve glycaemic control, reduce the risk of complications, and enhance the quality of life for pregnant women with diabetes. But to fully realize these benefits, the challenges of access, education and research must also be addressed. By further refining these technologies and expanding their use, we can further improve outcomes for both mothers and their newborns.

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