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Systematic Review

Does Continuous Glucose Monitoring Help in Pregnant Women?

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Abstract

Background: Diabetes is present in approximately 7% of all pregnancies. Maternal glucose control is a crucial issue. Evidence had demonstrated that optimal glycemic control during the first trimester could reduce congenital anomalies and perinatal mortality; likewise, during second and third trimester, it is also associated with reduced rates of pre-eclampsia, preterm delivery, large for gestational age and neonatal intensive care unit admissions. The aim of this review is to evaluate the current evidences about the glycemic control effects of continuous glucose monitoring (CGM) in pregnant women. **Methods**: We searched the PubMed database from January 1, 2011 to July 20, 2021, for English-language studies related to CGM uses in pregnancy. We mainly focused on randomized clinical trials (RCTs) and secondary analyses of RCT data. **Results**: After filtering, 14 researches were adopted by this study. We analyzed the results and sorted them into 4 main aspects, including difference between the outcomes of CGM users verses self-monitored blood glucose (SMBG) users, comparison of different modes of CGM, satisfaction of CGM, and using CGM to monitor glycemic levels in pregnant women under antenatal corticosteroids or ritodrine treatment. **Conclusions**: There is adequate evidence showing that CGM is effective at monitoring glycemic levels, improving maternal glycemia control as well as aiding with the insulin treatment, with more precise insulin dose.

Keywords: high risk pregnancy; diabetes mellitus; gestational diabetes mellitus; continuous glucose monitoring; self-monitored blood glucose

1. Introduction

Diabetes is present in approximately 7% of all pregnancies. Diabetes during pregnancy may be pre-existing (diabetes mellitus [DM]. type 1 or type 2) or gestational diabetes mellitus (GDM) [1]. Maternal glucose control is a crucial issue. Evidence had demonstrated that optimal glycemic control during the first trimester could reduce congenital anomalies and perinatal mortality [2,3]. Likewise, maintaining maternal glucose levels at acceptable range during second and third trimester is also associated with reduced rates of pre-eclampsia, preterm delivery, large for gestational age, and neonatal intensive care unit admissions [4–6].

In order to obtain appropriate blood glucose control, intensive multiple daily injections or continuous subcutaneous insulin infusion might be required [7]. Another key factor is frequent blood glucose monitoring. Traditionally, daily self-monitored blood glucose (SMBG) measurements and periodic HbA1c assessment were used to evaluate the sugar levels. However, inability to detect nocturnal glucose levels and postprandial hyperglycemic excursions limited its' effect on glycemic control [8,9].

Continuous glucose monitoring (CGM) is a novel device implanted in the subcutaneous layer to measure interstitial glucose level every 5 to 10 minutes and transfer the values to the external device [10]. CGM provides a more objective method of assessing the dynamic glucose levels throughout daily life [11]. It also provides immediate and retrospective effects of insulin treatment [10]. Improvement in glycemic control have been reported among patients with diabetes of the non-pregnant people [12]. Conflict results of CGM uses in pregnancy to improve neonatal outcome had also been reported [6]. In the 2021 American Diabetes Association standards, CGM is indicated to help achieving HbA1c targets and reduce neonatal hypoglycemia in pregnancy with type 1 DM [13].

The aim of this review is to evaluate the current evidences about the glycemic control effects of CGM in pregnant women. This review consists of comparing the difference between CGM and SMBG uses in terms of satisfaction of CGM, maternal outcomes, fetal outcomes, maternal glycemic profiles, and clinical/intervention utility. CGM use during antenatal corticosteroids administration is also reviewed.

2. Materials and Methods

We searched the PubMed database from January 1, 2011 to July 20, 2021, for English-language studies related to CGM use in pregnancy. We used the union sets of postpartum period, diabetes gestational, postnatal care,

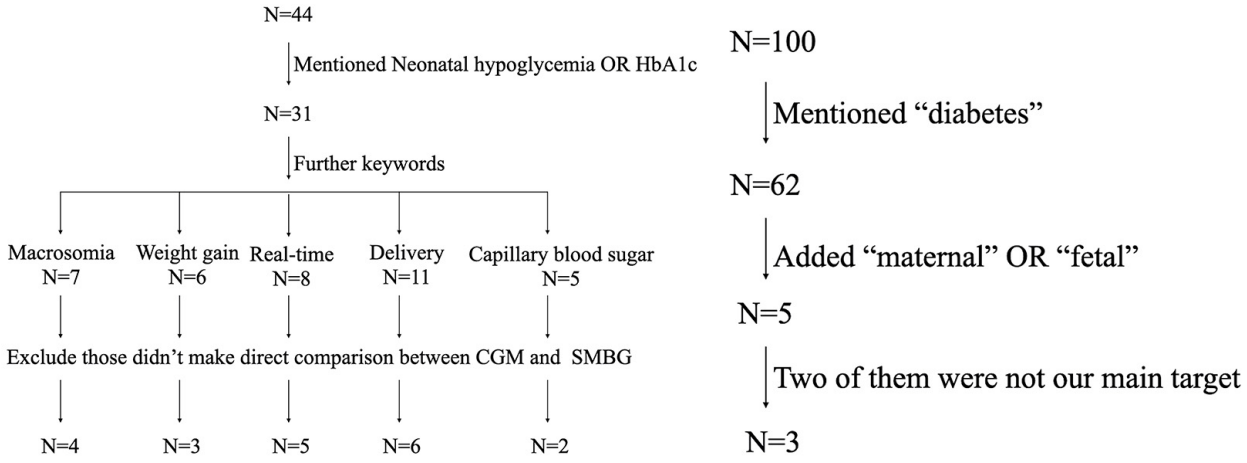

Fig. 1. Flowchart of paper selection.

preconception care, pregnancy, pre-existing diabetes and then crossed with CGM. Forty-four clinical trials were filtered according to terms mentioned above. Further keywords were added for specific topic review and 11 RCTs were selected (Fig. 1).

On the other hand, we applied tocolytic agents[MeSH Terms], adrenergic beta-agonists[MeSH Terms], steroids[MeSH Terms], ritodrine and tocolysis as keywords to get a union result; afterwards, we crossed it with continuous glucose monitoring and 100 manuscripts were showed. There were only 5 left after we added diabetes, maternal or fetal as filtering requirements (Fig. 1). Three of them were adopted by our review.

3. Results

After final filtering, 14 researches were adopted by this study. We analyzed the results and sorted them into 4 main aspects, including difference between the outcomes of CGM users verses SMBG users, comparison of different modes of CGM, satisfaction of CGM, and using CGM to monitor glycemic levels in pregnant women under antenatal corticosteroids or ritodrine treatment. The results will be presented in the following.

3.1 CGM Plus SMBG (CGM Users) vs. Controls (SMBG Users)

The outcomes are summarized into 4 groups, namely maternal glycemic profiles, maternal outcomes, fetal outcomes, and clinical/intervention utility.

3.1.1 Maternal Glycemic Profiles

3.1.1.1 HbA1c. Five RCTs and one RCT secondary analysis explored maternal HbA1c. Among RCTs, Feig *et al.* [14] demonstrated that CGM users showed significantly more improvement in HbA1c levels compared to baseline at 24 weeks and 34 weeks of gestation than SMBG users (GA 24 week: –0.67% vs. –0.52%, p = 0.0374/GA 34 week: –0.54% vs. –0.35%, p = 0.0372). Paramasivam *et al.* [15] demonstrated that CGM users showed significant lower HbA1c levels at gestational age 33 week and 37 week than SMBG users (GA 33 week: 5.1 $\pm$ 0.4 vs. 5.4 $\pm$ 0.6, p = 0.015/GA 37 week: 5.2 $\pm$ 0.4 vs. 5.6 $\pm$ 0.6, p = 0.006). Voormolen *et al.* [1] demonstrated no significant difference in HbA1c levels between two groups. In their subgroup analyses, different types of diabetes didn't show association between CGM use and HbA1c change as well. Secher *et al.* [16] and Wei *et al.* [17] both demonstrated no significant difference in HbA1c between CGM users and SMBG users throughout pregnancy. As for the RCT secondary analysis done by Yamamoto *et al.* [18], in newborns with neonatal hypoglycemia, the second and third trimester maternal HbA1c levels were significantly higher than those without hypoglycemia (HbA1c level in second trimester: 6.6 $\pm$ 0.6 vs. 6.2 $\pm$ 0.6, p = 0.0009/third trimester: 6.7 $\pm$ 0.6 vs. 6.3 $\pm$ 0.6, p = 0.0001).

3.1.1.2 Mean or Median Glucose . Three RCTs and two RCT secondary analyses reported the maternal mean or median blood glucose. Among RCTs, Petrovski *et al.* [10] showed that CGM users had significantly lower mean blood glucose compared to SMBG users (6.92 $\pm$ 2.1 mmol/L vs. 7.42 $\pm$ 3.4 mmol/L, p-value not shown) in first trimester, but there was no significant difference in mean glucose in second and third trimester between two groups. Paramasivam *et al.* [15] revealed no significant difference in fasting, pre-meals, postprandial glucose between CGM users and SMBG users throughout pregnancy. Secher *et al.* [16] also revealed no significant difference in median plasma glucose between CGM users and SMBG users at 8 and 33 weeks' gestational. Among RCT secondary analyses, Scott *et al.* [19] showed no difference in mean glucose between CGM users and SMBG users at any time during pregnancy; Cordua *et al.* [20] showed no difference in median self-monitored plasma glucose during the last 8 hours up to delivery between CGM users and SMBG users.

3.1.1.3 Time In Range, Time Above Range, Time Below Range. Three RCTs and two RCT secondary analyses explored time proportion spent in specific ranges. Among RCTs, Feig *et al.* [14] showed that CGM users had significantly higher percentage of time in range during pregnancy than SMBG users (68% vs. 61%, $p = 0.0034$). The CGM users also demonstrated significantly lower percentage of time above range than SMBG users (27% vs. 32%, $p = 0.0279$). There was no significant difference in time below range. Paramasivam *et al.* [15] revealed that patients with CGM has better glycemic control as pregnancy advances. Comparing glycemic status at 37 to 28 weeks' gestation, they spent more time in euglycemia (88.8 $\pm$ 7.0% vs. 84.6 $\pm$ 9.4%, $p = 0.016$) and less time in hyperglycemia (8.3 $\pm$ 6.3% vs. 12.7 $\pm$ 9.9%, $p = 0.017$). Nevertheless, Secher *et al.* [16] demonstrated no significant difference in time spent in euglycemia, hyperglycemia, and hypoglycemia between CGM users and SMBG users. Among RCT secondary analyses, Scott *et al.* [19] demonstrated that patients with CGM had significantly more time spent in glucose target range (67.6 $\pm$ 12.6% vs. 61.3 $\pm$ 15.5%, $p < 0.05$) and less time above the target (27.9 $\pm$ 13.4% vs. 33.1 $\pm$ 15.0%, $p < 0.05$) compared to patients with SMBG. Yamamoto *et al.* [18]. demonstrated that for newborns with neonatal hypoglycemia, maternal plasma glucose in second trimester spent significantly less time in normal range (46 $\pm$ 14% vs. 53 $\pm$ 15%, $p = 0.004$) and more time spent above range (50 $\pm$ 16% vs. 42 $\pm$ 17%, $p = 0.002$) than those without hypoglycemia. Similar results were also noted in third trimester (time percentage spent in range: 60 $\pm$ 16% vs. 66 $\pm$ 14%, $p = 0.03$; time percentage spent above range: 35 $\pm$ 16% vs. 29 $\pm$ 14%, $p = 0.01$).

3.1.1.4 Hypoglycemic Episodes. Three RCTs investigated maternal hypoglycemic episodes during pregnancy. Paramasivam *et al.* [15] revealed that CGM users showed significantly more hypoglycemic episodes, but no significant difference in "symptomatic hypoglycemia". Zhang *et al.* [21] demonstrated that ISGMS users had significantly less hypoglycemic events incidence than controls (5.45% vs. 21.82%, $p = 0.012$). Feig *et al.* [14] demonstrated no significant difference in hypoglycemic events between 2 groups.

3.1.1.5 Glycemic Variability. Two RCTs and one RCT secondary analysis reported the glycemic variability. Feig *et al.* [14] revealed that CGM users had significantly reduced glucose standard deviation (2.2 mmol/L vs. 2.4 mmol/L, $p = 0.0359$) and lower mean amplitude of glucose excursion compared to SMBG users (4.2 mmol/L vs. 4.6 mmol/L, $p = 0.0455$). Wei *et al.* [17] demonstrated that patients who wore CGM in the early stage had significantly lower mean amplitude of glucose excursions than those who wore it in the later stage (4.01 $\pm$ 0.14 mmol/L vs. 4.21 $\pm$ 0.45 mmol/L, $p = 0.046$). In RCT secondary analysis, Scott *et al.* [19] demonstrated that patients using CGM had significantly lower standard deviation (2.2 $\pm$ 0.5 mmol/L vs. 2.5 $\pm$ 0.7 mmol/L, $p < 0.05$) and coefficient of variation (32.5 $\pm$ 5.8% vs. 34.9 $\pm$ 7.6%, $p < 0.05$) than patients with SMBG.

3.1.2 Maternal Outcomes

3.1.2.1 Gestational Weight Gain . Five RCTs explored the effect of CGM on gestational weight gain and yielded inconsistent results. Feig *et al.* [14], Paramasivam *et al.* [15], and Secher *et al.* [16] demonstrated that there was no significant difference in gestational weight gain between CGM users and SMBG users. However, Zhang *et al.* [21] demonstrated that instantaneous scanning glucose monitoring system (ISGMS), which was similar to CGM, had advantage for control of gestational weight gain. 90.91% of patients with ISGMS (n = 50) achieved qualified weight gain in the end of pregnancy, which was defined by the individual's baseline weight. While only 70.91% of patients in controls (n = 39) achieved this. The difference was statistically significant. Wei *et al.* [17] demonstrated that CGM users has significantly less weight gain than those in the control group (13.56 kg $\pm$ 2.81 kg vs. 14.75 kg $\pm$ 2.91 kg, $p = 0.004$). Furthermore, the CGM users who used the CGMS in the second trimester gained less weight than those who used it during the third trimester (12.72 kg $\pm$ 2.83 kg vs. 14.31 kg $\pm$ 2.64 kg, $p = 0.003$).

3.1.2.2 Diabetic Ketoacidosis (DKA). Feig *et al.* [14] demonstrated no significant difference in DKA between CGM users and SMBG users.

3.1.2.3 Pregnancy-Induced Hypertension. Two RCTs explored the effect of CGM use on pregnancy-induced hypertension or worsening of chronic hypertension. Feig *et al.* [14] and Voormolen *et al.* [1] both revealed no significant difference in pregnancy-induced hypertension between CGM users and SMBG users.

3.1.2.4 Pre-Eclampsia. Three RCTs investigated the pre-eclampsia rate. Two of them (Feig *et al.* [14], Secher *et al.* [16]) demonstrated no significant difference in pre-eclampsia rate between CGM users and SMBG users, while Voormolen *et al.* [1] showed that pre-eclampsia risk was lower (relative risk, RR = 0.30, 95% confidence interval, CI = 0.12–0.80) for CGM users. Furthermore, subgroup analysis revealed statistically significant for type 1 DM and GDM, but not for type 2 DM.

3.1.2.5 HELLP Syndrome. Voormolen *et al.* [1] demonstrated that 4 of total 147 patients developed HELLP syndrome during pregnancy in the control group, while no patient developed this syndrome in CGM users (n = 143). This effect was not statistically significant.

3.1.2.6 Cesarean Section. Five RCTs and one RCT secondary analysis explored the cesarean section rate. All five RCTs (Feig *et al.* [14], Voormolen *et al.* [1], Paramasivam *et al.* [15], Secher *et al.* [16], Wei *et al.* [17]) reported no group difference between CGM and SMBG users in cesarean section rate. On the other hand, Yamamoto *et al.* [18] conducted a RCT secondary analysis revealing that higher cesarean section rate was reported in newborn with neonatal hypoglycemia compared with no hypoglycemia (83% vs. 64%, $p = 0.01$).

3.1.2.7 Miscarriage. Secher *et al.* [16] demonstrated that there was no significant difference in miscarriage rate between two groups.

3.1.3 Fetal Outcomes

3.1.3.1 Birth Weight. Four RCTs and two RCT secondary analyses explored the birth weight of neonates. Among RCTs, Voormolen *et al.* [1], Paramasivam *et al.* [15], Secher *et al.* [16], Wei *et al.* [17] demonstrated no significant difference in birth weight between CGM users and SMBG users. In RCT secondary analyses, Yamamoto *et al.* [18] revealed no significant difference in birth weight between newborns with or without neonatal hypoglycemia. But the birth weight centile was significantly higher for newborns with neonatal hypoglycemia than those without hypoglycemia (89 ± 22 vs. 80 ± 26, $p = 0.02$). Cordua *et al.* [20] found no significant difference in newborn birth weight between CGM use and SMBG use during labor and delivery.

3.1.3.2 Large for Gestational Age (LGA). Five RCTs and two RCT secondary analyses explored the rate of LGA. Among RCTs, Feig *et al.* [14] revealed that CGM users demonstrated significantly lower rate of LGA (53%) than SMBG users (69%). However, other four RCTs included Voormolen *et al.* [1], Paramasivam *et al.* [15], Secher *et al.* [16], Wei *et al.* [17] demonstrated no significant difference in LGA rate between two groups. Among RCT secondary analyses, Yamamoto *et al.* [18] demonstrated significantly higher rate for LGA in newborns with neonatal hypoglycemia (74%) than those without neonatal hypoglycemia (58%). Cordua *et al.* [20] found no significant different in LGA between CGM use and SMBG use during labor and delivery.

3.1.3.3 Macrosomia. Four RCTs investigated the rate of macrosomia, which was defined as birth weight above the 90th centile. Feig *et al.* [14], Voormolen *et al.* [1], Wei *et al.* [17] demonstrated no significant difference in macrosomia between CGM users and SMBG users. In Paramasivam *et al.*'s study [15], there was no macrosomia detected in both groups.

3.1.3.4 Shoulder Dystocia. Voormolen *et al.* [1] demonstrated no significant difference in shoulder dystocia rate between CGM users and SMBG users.

3.1.3.5 Small for Gestational Age (SGA) . Four RCTs and one RCT secondary analysis investigated the rate of SGA. Among RCTs, Feig *et al.* [14], Voormolen *et al.* [1], Wei *et al.* [17] revealed no significant difference in SGA between CGM users and SMBG users. In study conducted by Paramasivam *et al.* [15], no SGA was detected in both CGM users and SMBG users. Among RCT secondary analysis, Yamamoto *et al.* [18] demonstrated no significant difference in SGA between newborns with or without neonatal hypoglycemia.

3.1.3.6 Neonatal Hypoglycemia. It has been well known that maternal hyperglycemia results in fetal hyperglycemia and hyperinsulinemia. These could lead to neonatal hypoglycemia after delivery because of the discontinuance of glucose supply from hyperglycemic maternal blood [22]. Five RCTs and one RCT secondary analysis investigated the rate of neonatal hypoglycemia. Among RCTs, Feig *et al.* [14] revealed that CGM users demonstrated significantly lower rate of neonatal hypoglycemia (15%) than SMBG users (28%). However, other four RCTs included Voormolen *et al.* [1], Paramasivam *et al.* [15], Secher *et al.* [16], Wei *et al.* [17] demonstrated no significant difference in neonatal hypoglycemia rate between CGM users and SMBG users. In one RCT secondary analyses, Cordua *et al.* [20] found no significant different in LGA between CGM use and SMBG use during labor and delivery.

3.1.3.7 Neonate 2-hour Plasma Glucose. One RCT and one RCT secondary analysis explored neonate 2-hour plasma glucose. Both Secher *et al.* [16] and Cordua *et al.* [20] demonstrated no significant difference in neonate 2-hour plasma glucose between CGM users and SMBG users.

3.1.3.8 Gestational Age (GA) At Delivery. Two RCTs and two RCT secondary analyses reported gestational age at delivery. Paramasivam *et al.* [15] and Secher *et al.* [16] demonstrated no significant difference in gestational age at delivery between CGM users and SMBG users. Among RCT secondary analyses, Yamamoto *et al.* [18] demonstrated significantly less gestational age for newborns with neonatal hypoglycemia than those without neonatal hypoglycemia (36.2 ± 1.7 vs. 37.2 ± 1.6, $p = 0.0002$). Cordua *et al.* [20] found no significant different in gestational age at delivery between CGM use and SMBG use during labor and delivery.

3.1.3.9 Preterm Delivery. Preterm delivery, which indicated deliveries before gestational age of 37 weeks. Four RCTs, namely Feig *et al.* [14], Voormolen *et al.* [1], Paramasivam *et al.* [15], and Secher *et al.* [16] and two RCT

secondary analyses explored the rate of premature delivery. All four RCTs [1,14–16] and Cordua *et al*. [20] demonstrated no significant difference in premature delivery between CGM and SMBG users. On the other hand, Yamamoto *et al*. [18] found that newborns with neonatal hypoglycemia had higher risk of prematurity (63%) than those without hypoglycemia (32%).

3.1.3.10 Respiratory Distress Syndrome (RDS). Feig *et al*. [14]. demonstrated that no significant difference in newborn RDS between CGM users and SMBG users.

3.1.3.11 Neonatal Intensive Care Unit (NICU) Admission. Two RCTs and one RCT secondary analysis explored the rate of NICU admission for newborns. Among RCTs, Voormolen *et al*. [1] and Paramasivam *et al*. [15] both revealed no significant difference in NICU admission between CGM users and SMBG users. Yamamoto *et al*. [18] demonstrated that newborns with neonatal hypoglycemia had higher rate of NICU admission (90%) than those without neonatal hypoglycemia (19%).

3.1.3.12 NICU Stay. Feig *et al*. [14] demonstrated that significantly less rate for NICU stay >24 hours in newborns of CGM users (27%) than those of SMBG users (43%).

3.1.3.13 Length of Stay. Feig *et al*. [14] demonstrated that significantly less days for infant length of stay in newborns of CGM users than those of SMBG users (3.1 vs. 4.0, p = 0.0091).

3.1.3.14 Hyperbilirubinemia. Feig *et al*. [14] demonstrated that no significant difference in newborn hyperbilirubinemia between CGM users and SMBG users.

3.1.3.15 Neonatal Jaundice. Paramasivam *et al*. [15] demonstrated that no significant difference in neonatal jaundice between CGM users and SMBG users.

3.1.3.16 Neonatal Death. Voormolen *et al*. [1] demonstrated one neonatal death for both CGM users and SMBG users. Paramasivam *et al*. [15] demonstrated no neonatal death for both CGM and SMBG users.

3.1.3.17 Congenital Malformation. Voormolen *et al*. [1] demonstrated no significant difference in major congenital malformation between CGM users and SMBG users. Paramasivam *et al*. [15] demonstrated no fetal anomaly for both CGM and SMBG users.

3.1.3.18 Apgar Score at 5 Minutes. Wei *et al*. [17] found no significant different in Apgar score at 5 minutes between CGM users and SMBG users.

3.1.4 Clinical/Intervention Utility

3.1.4.1 The Need of Insulin and the Dose Required. Three RCTs and two RCT secondary analyses reported the Insulin usage and required dose. Among RCTs, Wei *et al*. [17]. revealed that insulin was significantly more commonly used in CGM group than in SMBG group (31.3% vs. 12.7%, p = 0.02), while there was no significant difference in insulin dose between two groups. Feig *et al*. [14] demonstrated no significant difference in daily insulin dose and rate of changing to insulin pump between CGM users and SMBG users. Insulin pump, which is a device that can help to infuse insulin in the manner of how human pancreas work. Paramasivam *et al*. [15] demonstrated that no significant difference was revealed between CGM users and SMBG users in terms of the initiation, duration, and required dose of insulin therapy. Among RCT secondary analyses, Yamamoto *et al*. [18] reported that significantly higher rate of insulin pump use was presented by mothers whose newborn had neonatal hypoglycemia, compared to those without neonatal hypoglycemia (61% vs. 45%, p = 0.03). Cordua *et al*. [20] demonstrated no significant difference between CGM users and SMBG users in terms of proportion of insulin pump use and required insulin dose.

3.1.4.2 OAD (Oral Antidiabetic Drug). Paramasivam *et al*. [15] revealed no significant difference in metformin therapy between CGM users and SMBG users in terms of the timing of initiation, duration, or required dose.

3.1.4.3 Compliance with Blood Glucose Monitoring. Zhang *et al*. [21] demonstrated that patients with ISGMS had higher compliance compared to the control group (94.55% vs. 74.55%, p = 0.004).

3.1.4.4 Health Behavior Patterns. Zhang *et al*. [21] demonstrated that patients with ISGMS had superior health behavior patterns compared to the control group. These difference included superior blood glucose monitoring, diet control, weight monitoring, appropriate exercise, and regular obstetric checkups (p = 0.000, 0.008, 0.002, 0.006, and 0.019, respectively).

3.2 Comparison of Different Modes of CGM

Lane *et al*. [23] conducted a randomized controlled trial which compared the blood glucose control between women with GDM using real-time CGM (n = 12) or blinded CGM (n = 11). The real-time CGM could display current blood glucose and the trend of levels in the past several hours, while data of the blinded CGM could be read retrospectively by downloading through a computer system. The women with blinded CGM were blinded to the CGM data and interventions were based on their SMBG values. All participants were evaluated for 4 weeks. The results revealed no significant difference the mean blood glucose in the fourth week. As for other blood glucose parameters,

there were no significant difference in time in range, time above range, time below range, and HbA1c. The number of patients requiring medications was comparable. Both groups had similar maternal outcomes included body mass index at delivery, gestational hypertension, pre-eclampsia, polyhydramnios, cesarean delivery, operative vaginal delivery, third- or fourth-degree laceration. There were still no significant difference between two groups for any fetal outcomes included gestational age at delivery, preterm birth, birth weight, LGA, SGA, NICU admission, RDS, shoulder dystocia, macrosomia.

Petrovski *et al.* [10] conducted a pilot study which randomizely compared the glycemic control between women with type 1 DM using constant CGM (n = 12) or intermittent CGM (n = 13). Women with constant CGM used CGM continuously, while women with intermittent CGM used CGM 1 week with sensor and 1 week without sensor. The results demonstrated that HbA1c (6.52 $\pm$ 1.3% vs. 6.82 $\pm$ 0.7%, $p < 0.05$) and mean blood glucose (6.92 $\pm$ 2.1 mmol/L vs. 7.42 $\pm$ 3.4 mmol/L, $p < 0.05$) of the constant group were significantly lower than intermittent group in first trimester. However, in trend cannot be seen in the second and third trimester. The required dose of insulin for both groups were comparable. When it comes to maternal outcomes, intermittent group showed more hypoglycemic episodes (2 vs. 1, *p*-value not shown) and DKA (1 vs. 0, *p*-value not shown) than constant group. There was no significant difference in gestational weight gain, cesarean section. The fetal outcomes included preterm delivery, macrosomia, neonatal hypoglycemia were all similar between both groups.

3.3 Satisfaction of CGM

Two RCTs reported satisfaction of CGM demonstrated that these devices were well-accepted. Feig *et al.* [14] demonstrated that patients with CGM showed overall favorable ratings on satisfaction scores (mean = 3.66–3.78 on a 4-point scale). Lane *et al.* [23] demonstrated that all patients thought that CGM did not negatively affect their quality of life. All patients felt that continuous feedback of real-time CGM enabled them to have better food choices. Although one-third (34%) of patients reported adverse effects like redness, pain, tenderness, or swelling at sensor insertion site, all of which could be relieved by changing the insertion site.

3.4 CGM in Pregnant Women Using Antenatal Corticosteroids or Ritodrine

Refuerzo *et al.* [24] conducted an observational pilot study using CGM to compare the maternal glycemic control after antenatal corticosteroids administration in pregnancy with or without DM. Six DM women and three non-DM women participated this study. The results revealed that the median blood glucose of DM women after corticosteroids administration at 20, 44, 68 hours were higher but not statistically significant than non-DM women. During the CGM monitoring period (72 hours), the blood glucose of DM women raised 33% to 48% from baseline and the non-DM women raised 16–33% in response to corticosteroids. The required doses of insulin were increased for DM women while no insulin was required for non-DM women.

Langen *et al.* [25] conducted a prospective observational study using CGM to demonstrate maternal glucose response to corticosteroids administration. They recruited 11 non-DM and 4 DM pregnant women who were indicated to receive betamethasone between 24 to 34 weeks' gestation. The result revealed that DM women spent similar time in hyperglycemia compared with non-DM women during the first 48 hours post steroid administration.

Itoh *et al.* [26] retrospectively analyzed the blood glucose pattern of 12 pregnancies with GDM who received antenatal corticosteroids treatment. There were 8 patients who also received ritodrine for preterm labor. The blood glucose levels were measured by CGM. The dose of insulin required were increased after betamethasone administration. There were time-dependent changes in insulin requirement after adjusting for maternal body weight. The total insulin requirement in those with ritodrine was significantly higher than those without ritodrine (130.8 $\pm$ 15.0 vs. 76.8 $\pm$ 15.2 units/day, $p < 0.05$). There were no adverse effects such as severe hypoglycemia, DKA, symptomatic hypokalemia during treatment.

4. Discussion

In this review, we found benefits in glycemic control under CGM use compared to SMBG use only [14,15,19,21]. CGM use could improve glycemic control by keeping glucose levels in target range, decreasing glycemic variability, and in turn keeping HbA1c in lower levels. Also, most patients showed positive attitude to the use of CGM for monitoring their blood sugar [14,23]. However, when it comes to maternal or fetal outcomes (Table 1), no such difference were seen. The reason may be that those outcomes are related to multiple factors rather than maternal blood sugar alone. Also, difference in recruited population, duration of CGM use, and relatively small population could also contribute to the result.

For effects on the mother, we found equivocal findings between different studies. Generally no difference among each outcome was revealed by the majority of the studies. The two studies in Chinese population [17,21] demonstrated that gestational weight gain could be decreased by CGM use compared with SMBG use in pregnant women having GDM, while Paramasivam *et al.* [15], with the similar population, showed no weight-control effect. The distinct duration of CGM use may contribute to this difference. In Zhang *et al.* [21] and Wei *et al.*'s studies[17], CGM was used for an entire trimester or from randomization to delivery, while Paramasivam *et al.* [15] designed patients to

Table 1. Diabetes-related complications.

Maternal	Neonatal
Excessive weight gain	Large for gestational age
Diabetic ketoacidosis	Macrosomia
Pregnancy induced hypertension	Small for gestational age
Preeclampsia	Shoulder dystocia
HELLP syndrome	Neonatal hypoglycemia
Increase Cesarean section rate	Preterm delivery
Miscarriage	Respiratory distress syndrome
	Neonatal jaundice
	Neonatal death
	Congenital malformation

receive CGM intermittently. Continuous use of CGM may let the patients be more watchful on her own glucose and weight control.

In terms of fetal outcomes, no significant difference in fetal outcomes was generally found among CGM users and SMBG users.

There were two aspects in comparison of CGM mode. One is real-time versus retrospective, and the other is constant versus intermittent. In our review, the sample size of RCT done by Lane *et al*. [23] was too small to conclude the difference of real-time CGM versus retrospective CGM. In terms of constant CGM, Petrovski *et al*. [10] showed that the glycemic control was better with improved HbA1c and mean blood glucose. Besides, rates of DKA and severe hypoglycemia were also decreased in constant group. However, the sample size of this study was still not adequate to confirm the findings.

CGM was also used to monitor glycemic levels during corticosteroid treatment and the perinatal period of pregnant woman. The blood glucose levels typically elevated after corticosteroids administration and the perinatal period [24, 25]. The effect of insulin treatment could be appropriately adjusted under the aid of CGM use [26]. The CGM use in these timing seemed plausible and effective. Yet the fetal outcomes such as neonatal hypoglycemia, NICU admission were not explored, which could be investigated by future studies.

5. Conclusions

There is adequate evidence showing that CGM is effective at monitoring glycemic levels, improving maternal glycemia control as well as aiding with the insulin treatment, with more precise insulin dose. The inconsistent findings between different studies might be owing to varied population(including different ethnics, different DM types and other underlying medical conditions) and distinct duration and modes of CGM use. The comparison between different CGM mode and the CGM effect during antenatal corticosteroids to perinatal period need further study with larger sample size to investigate.

Author Contributions

TFC designed the research study. JAH performed the research and analyzed the data. WYH and ICS wrote the manuscript. TFC provided help and advice on paper inclusion and reviewing. All authors contributed to editorial changes and amendment in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. TFC is serving as the guest editor of this journal. We declare that TFC had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to LR and SM.

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