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ABSTRACT

Objective

To evaluate glycaemic profiles in uncomplicated pregnancies using continuous glucose monitoring (CGM) and examine how these profiles correlate with birth weight (BW).

Design

This was a prospective observational study including 89 singleton pregnancies to identify normal glycaemic profiles in women experiencing physiological changes in glucose homeostasis.

Methods

Participants were randomly selected, with inclusion criteria limited to women with uncomplicated pregnancies (no pre-existing conditions, hypertensive disorders, or diabetes). Maternal demographic data, including age, parity, ethnicity, smoking habits, and method of conception, were recorded at first visit. CGM (Dexcom G6 system) was used for 10 days each time, at three time points (11-14, 26-28, and 35-37 weeks) and maternal biophysical measurements were collected at the above time points 42 of these patients went on to develop gestational diabetes mellitus (GDM). The CGM metrics analysed were mean glucose, glucose variability (GV), time in range (TIR 3.5-7.8mmol/L), time above range (TAR >7.8mmol/L), time below range (TBR < 3.5 and < 3.0mmol/L) and glucose management indicator (GMI). Neonatal BW was measured to the nearest gram and BW centiles were calculated based on gestation and BW.

Introduction

CGM is commonly used in clinical practice, outside pregnancy, to help manage diabetes and it is known to improve diabetic complications (1). TIR correlates with HbA1c and is linked to microvascular complications and GV has shown to be associated with cardiovascular disease and peripheral neuropathy (2,3), while TBR and TAR support treatment adjustments and monitor compliance (4–6). The immediate CGM feedback has shown to encourage healthy behaviours and promote accountability (5).

CGM is now becoming widely used in pregnancy to help monitor glycaemic profiles in women with pre-existing diabetes (mainly T1DM). Despite the increasing use of CGM, its integration into routine clinical practice has been limited, primarily because of the absence of clear ‘normal’ pregnancy glycaemic reference targets/ranges for healthcare providers and patients to work towards (1). While there is clear evidence supporting the use of CGM in pregnant women with T1DM, there is less evidence for those with T2DM and GDM and although the same glucose ranges may be used for TIR, TAR and TBR the specific percentages for each parameter have yet to be established (1). In summary, there is little knowledge on what a CGM glycaemic profile looks like in low-risk uncomplicated pregnancies and how these metrics can be associated with pregnancy outcomes.

Results

CGM-derived mean glucose levels were stable across trimesters, averaging at 6.0 mmol/L. Women spent a median of 92% of their TIR (3.5-7.8 mmol/L), which was stable during the first two trimesters with a decrease by the third trimester. A median of 6% (86 minutes) of time was spent above range (>7.8 mmol/L) and 21 minutes were spent below range (<3.5 mmol/L and <3.0mmol/L) over a 24-hour period.

After undergoing Ordinary Least Square (OLS) regression analysis, and adjusting for maternal baseline characteristics, we found that in the first trimester, a 1 mmol/L increase in mean glucose was associated with a 144 g increase in BW (p = 0.03) and 1% rise in GMI correlated with a 247 g BW increase (p = 0.01). In the second trimester, a 1% increase in TIR reduced BW by 9 g (p = 0.05), while a 1% increase in TAR raised BW by 8 g (p = 0.05). In the third trimester, a 1 mmol/L increase in mean glucose led to a 1.6% rise in neonatal fat mass (p = 0.03).

CGM Variables	First Trimester (11-14 weeks)	Second Trimester (26-28 weeks)	Third Trimester (35-37 weeks)	Entire Gestational Period
Number of days CGM worn (days)	10.00 (8.50 – 10.00)	9.40 (9.00 – 9.90)	9.00 (8.39 – 9.90)	9.40 (8.39 - 10.00)
Percentage time CGM active (%)	99.20 (95.30 – 100.0)	98.80 (96.26 – 100.0)	98.40 (95.60 – 100.0)	99.00 (95.60 - 100.00)
Mean glucose (mmol/L)	5.90 (5.60 – 6.20)	5.96 (5.40 - 6.10)	6.01 (5.70 - 6.10)	5.96 (5.50 - 6.20)
Percentage glycaemic variability (%)	17.50 (15.75 - 19.35)	18.70 (16.00 - 20.79)	19.70 (17.85 - 21.06)	18.50 (16.30 - 21.06)
Percentage time in range (%)	94.00 (89.95 - 96.05)	92.00 (88.00 - 96.45)	87.60 (86.80 - 93.15)	91.80 (87.60 - 95.30)
Percentage time above range (%) (>7.8mmol/L)	4.00 (2.00 – 7.55)	6.00 (1.35 - 10.18)	9.10 (4.20 - 10.93)	6.00 (2.40 - 10.70)
Percentage time below range (%) (<3.5 mmol/L)	0.90 (0.20 - 1.00)	1.00 (0.50 - 1.40)	1.30 (0.50 - 1.71)	1.00 (0.50 - 1.71)
Percentage time below range (%) (<3.0mmol/L)	0.50 (0.10 - 1.00)	0.50 (0.10 - 0.78)	1.00 (0.20 - 1.03)	0.50 (0.10 - 1.00)
Glucose management indicator (A1C%)	5.60 (5.40 - 5.80)	5.60 (5.40 - 5.70)	5.63 (5.40 - 5.70)	5.60 (5.40 - 5.70)

Table: Descriptive statistics of trimester-specific CGM glucose profiles. Data are expressed as median (Interquartile Range)

CGM metric	Pregnancy Outcome	Effect Estimate ± Standard Error	p-value	Interpretation
1st Trimester				
Mean Glucose (mmol/L)	BW (g)	+144.21 ± 63.78 g	0.03	↑ glucose → ↑ BW
GMI (%)		+246.88 ± 95.63 g	0.01	↑ GMI → ↑ BW
2nd Trimester				
% TIR (3.5-7.8mmol/L)	BW (g)	-8.58 ± 4.29 g	0.05	↑ TIR → ↓ BW
% TAR (>7.8mmol/L)		+8.27 ± 4.14 g	0.05	↑ TAR → ↑ BW
3rd Trimester				
Mean Glucose (mmol/L)	Neonatal fat mass (%)	+1.63 ± 0.72%	0.03	↑ mean glucose → ↑ neonatal fat mass

Table: Summary of key statistical findings following OLS models assessing the relationship between trimester-specific CGM measurements and pregnancy outcomes

Discussion and conclusions

This study describes the ‘normal’ range of CGM during gestation in singleton, uncomplicated pregnancies. In uncomplicated pregnancies, the CGM-derived metrics demonstrated stable mean glucose levels across trimesters and the preservation of a high TIR (> 90%) and minimal TAR/TBR offering a physiological benchmark, a reference glycaemic phenotype for uncomplicated pregnancies.

The findings in this study also suggest significant effects of trimester-specific CGM metrics on pregnancy outcomes such as BW which aligns with existing literature by Scott et al. and the HAPO study, which show that maternal glycaemic profiles influence pregnancy outcomes (7,8) and that early pregnancy glycaemic profiles, even at glucose levels below current diagnostic thresholds for GDM, are linked to maternal and neonatal outcomes (9), emphasising the importance of early screening and intervention.

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