COMMENTARY

Longitudinal Continuous Glucose Monitoring Metrics During Healthy Pregnancy and Following Gastric Bypass

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Pregnancies after Roux-en-Y gastric bypass (RYGB) are increasing as obesity rates continue to rise among women of reproductive age. The study by Stentebjerg et al. (1) highlights the striking reduction in prepregnancy BMI from 45 kg/m^2 (interquartile range 42–54 kg/m^2) to 32 kg/m^2 (interquartile range 27–39 kg/m^2) approximately 2.5 years following RYGB in women aged 29 years. An average weight loss of ∼50 kg with an estimated 80% reduction in excess body weight improves fertility and reduces complications of future pregnancy for both mother and child (2). The most common side effect of RYGB is exaggerated postmeal glucagon-like peptide 1 (GLP-1) and plasma insulin responses, which contribute to postprandial hypoglycemia (3). This phenomenon, known as postbariatric hypoglycemia (PBH), is defined as glucose level <3.3 mmol/L (59 mg/dL). PBH has been associated with female sex and younger age at RYGB and may be further exacerbated by β-cell hyperplasia during pregnancy. It is commonly observed during an oral glucose tolerance test for diagnosing gestational diabetes mellitus (GDM).

PBH has been reported in up to 58% of pregnant women previously treated with RYGB, but whether it contributes to intrauterine growth restriction is unknown (4). Stentebjerg et al. (1) describe the glycemic profiles from a prospective observational Bariatric Surgery and Consequences for Mother and Baby in Pregnancy (BAMBI) study of 23 women with RYGB and 23 weight-matched control participants. Participants wore a continuous glucose monitor (CGM) in each trimester (14, 24, and 36 weeks gestation) and 4–6 weeks postpartum.

A key contribution is the novel description of longitudinal CGM glycemic metrics in a healthy control population. Control participants (aged 30 years, BMI 33 kg/m^2, 60% primiparous) had ∼96% time in the target glucose range (TIR) (3.5–7.8 mmol/L, 63–140 mg/dL) during the first and second trimesters, dropping to ∼94% at 36 weeks and postpartum. The corresponding time above range (TAR) (>7.8 mmol/L, 140 mg/dL) increased from ∼4–6% at 36 weeks and postpartum. Mean CGM glucose levels were 5.8–6.0 mmol/L (104–108 mg/dL) during the day (0600–2359 h) and overnight (2400–0559 h) throughout pregnancy. Time below range (TBR) (<3.5 mmol/L, 63 mg/dL) and glycemic variability (glucose coefficient of variation [CV]) were both remarkably low (TBR <1%, CV 15%). The median nocturnal CGM glucose of 6.0 mmol/L (108 mg/dL) obtained by BAMBI control participants under free-living conditions is appreciably higher than the 4.5 mmol/L (81 mg/dL) from fasting plasma glucose samples (5). Glycemic patterns are otherwise comparable to those in women with risk factors for GDM from the Study of Pregnancy Regulation of Insulin and Glucose (SPRING) (5). These data will inform future consensus regarding clinical CGM targets in healthy and GDM pregnancies.

In contrast, women with previous RYGB had significantly lower TIR ∼87–90% throughout pregnancy and postpartum. This was mainly due to higher TAR, which was 9.0–10% (2–2.5 h per day hyperglycemic) during pregnancy, rising to 12% postpartum. TBR <3.5 mmol/L was 1.5–3.0% (20–45 min) during pregnancy, with approximately 10–15 min recorded at <3.0 mmol/L (54 mg/dL). Given the limited accuracy of sensors, loose abdominal skinfolds after RYGB, and short duration in the low-glucose range, TBR data should be interpreted with caution. Interestingly, there were no between-group differences in mean 24-h sensor glucose concentrations for healthy versus RYGB participants, although glycemic variability was significantly higher (CV 25–27%), most likely reflecting postprandial hyperglycemia after RYGB. An unexpected finding was the low median nocturnal glucose levels in RYGB participants (nadir 4.9 mmol/L or 88 mg/dL), while the levels increased across gestation in healthy control participants. This decreasing nocturnal glucose pattern in

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late pregnancy among mothers with previous RYGB procedures is of unknown clinical relevance.

Pregnancy outcomes were largely reassuring, with >95% of deliveries at term (between 38 [±2] and 40 [±1] weeks), 100% vaginal or elective caesarean deliveries, and median neonatal birth weight 3,365 g. Four babies (17%) were admitted to neonatal care units in each group, suggesting no differences in clinically relevant neonatal morbidity, although the indication(s), duration, and level of neonatal care were not explicitly stated. The median birth weights and corresponding birth weight centiles were numerically lower in RYGB neonates without significant differences in neonatal anthropometrics or in rates of large for gestational age (LGA) or small for gestational age (SGA). The expected continuous relationship between maternal glucose and neonatal birth weight was confirmed in both groups, with lower median glucose in mothers who subsequently delivered an SGA baby and higher median glucose in those with an LGA baby.

The glycemic metrics of 20 mothers who delivered babies of appropriate-for-gestational-age (AGA) birth weight are of interest, with mothers of AGA babies in the control group having 96% TIR and 4% TAR compared with 87% TIR, 10% TAR, and 3% TBR in those with RYGB. The key difference in glycemic metrics is the increasing TAR, rising from 7–11% across increasing birth weight categories from SGA to LGA among RYGB mothers. The TBR metrics, specifically time spent below 3.5 mmol/L and 3.0 mmol/L (63 mg/dL and 54 mg/dL), were 3% and 1%, respectively, among RYGB mothers with both AGA and SGA babies. Dichotomizing continuous birth weight variables according to the highest or lowest 10th percentile is challenging in small study populations, so any comparisons between the six SGA and three LGA neonates of RYGB mothers should be interpreted with appropriate caution. This is also true for dichotomizing glycemic metrics, particularly at the low sensor glucose range, where data points are limited.

Among RYGB participants, hyperglycemia and glycemic variability were approximately twofold higher both throughout pregnancy and postpartum with 1–3% TBR. The consequences of spending 15–45 min with low sensor glucose without clinical symptoms is unknown. It is unclear whether these were reactive hypoglycemic events following postprandial hyperglycemia and whether they were potentially modifiable with dietary adjustments. Two women with previous RYGB had repeated clinical hypoglycemia events leading to their driving licenses being revoked. These women may benefit from using real-time CGM with alarm features during future pregnancies.

The international consensus on proposed targets for CGM metrics during pregnancy were based on values largely derived from type 1 diabetes (T1D) in pregnancy (6–8). While most BAMBI control participants were overweight and obese (BMI 33 kg/m^2), they nonetheless provide important insights into the CGM glycemic profiles during healthy pregnancy, suggesting favorable neonatal outcomes in mothers with 96% TIR, 4% TAR, median glucose 6.0 mmol/L, and CV 15%. Interestingly, there were no differences between median glucose during the daytime and nighttime, suggesting that CGM mean/median glucose targets are applicable across the 24-h day. This is similar to recent T1D pregnancy findings where normal birth weight was associated with lower mean CGM glucose and higher TIR across the 24-h day (9).

The availability of CGM has challenged our understanding of sensor-detected versus person-reported hypoglycemic events. More work is needed to understand the risks and benefits of higher TBR during and outside of pregnancy. While small changes in maternal glucose undoubtedly influence fetal growth trajectories, the relative contributions of lower nocturnal glucose, PBH, and/or malabsorptive bypass surgery to intrauterine growth restriction warrant further investigation. Meanwhile, pregnant women with previous RYGB should be reassured that 50 kg prepregnancy weight loss far outweighs any concerns of sensor-detected hypoglycemia. More data regarding CGM metrics in healthy pregnancy are needed, but these data suggest that 96% TIR, 4% TAR, median glucose 6.0 mmol/L (108 mg/dL), and CV 15% are applicable.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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