# Chapter 3: Later timing of eating and longer fasting duration during pregnancy is associated with lower infant birth weight and greater parent glycemia

## Abstract

The timing of eating and duration of overnight fast are emerging components of the diet that are gaining popularity as factors to manipulate for health reasons. Little research has been conducted on the timing of eating in pregnant populations, despite pregnancy being recognized as a critical period in development. We assessed the relationship between the timing of eating and duration of fasting during the second and third trimester of pregnancy and parent mid-gestation oral glucose tolerance test results and infant birthweight. In 102 parent-child dyads of the Pregnancy Related Eating Sleeping and Stress (PRESS) study, we found that later timing of first meal and later fasting midpoint in trimester 2 was associated lower birth weight. During the third trimester, significantly lower infant birth weight in relation to fasting duration and fasting midpoint were attenuated when individuals who delivered preterm were excluded from the analysis. Later timing of first meal in the second and third trimesters were associated with slightly higher OGTT test values. These data suggest that the timing of eating and duration of fasting during pregnancy could be important and under-recognized components of eating behavior that impact perinatal health.

## Introduction

There are few times in life when nutritional intake matters as much as during the course of pregnancy. Modern science has demonstrated that pregnancy is a critical period of vulnerability that can impact trajectory toward health or disease, in both the birthing parent and the child. As such, much attention has been paid in scientific discourse on identifying modifiable behaviors that can improve the likelihood that results in a healthy pregnancy. The majority of the research in nutrition on this topic are focused on dietary quality, and nutrient adequacy. It is unsurprising that caloric restriction and poor diet quality are both strongly associated with worse outcomes in both parents and children (Marshall et al., 2022). However, recent evidence has pointed toward a previously under-recognized modifiable component of the diet, the timing and duration of eating.

Initial evidence about the impact of the timing of eating on human health came from the field of sleep research. Routinely, researchers found that workers whose shifts are in opposition to the normal circadian rhythm have greater risks of ill health, including higher rates of miscarriage (Begtrup et al., 2019), pre-term birth (Cai et al., 2019; Davari et al., 2018), and odds of developing preeclampsia (Cai et al., 2019).

New attention has been called to all health behaviors that impact or are impacted by one’s circadian rhythm. As such, modifying or compressing the timing of ones eating schedule is gaining popularity as a way to modulate health. One such modality is time-restricted eating. Evidence from human studies finds that condensing the eating window is effective for weight loss (Gabel et al., 2018; Hutchison et al., 2019; Lowe et al., 2020). There have also been studies that find that metabolic health markers, such as blood pressure and cholesterol can be improved from TRE without the reduction in body weight (Sutton et al., 2018). However, experimental data from human pregnant populations does not currently exist and observational evaluations are extremely limited.

These few studies that evaluate the timing of eating in relation to perinatal health in humans find that there are small, but significant elevations in parent fasting glucose when fasting duration is greater during pregnancy (Loy et al., 2017). There is also evidence that eating earlier in the day during pregnancy is associated with more favorable dietary quality (Gontijo et al., 2020). Interest in this topic is mounting as future cohort studies are planned to further assess the role of chronobiology and timing of meals during pregnancy on perinatal health outcomes (Kaur et al., 2020). One study has also investigated the attitudes surrounding engaging in time-restricted eating during pregnancy. In their population of pregnant or recent post-partum parents nearly 25% reported they would be open to trying this modality during pregnancy to improve health (Flanagan et al., 2022). Although, not all participants endorsed the diet as appropriate for pregnancy. There is also a clinical case study that employed intermittent fasting to improve postprandial blood glucose concentrations in a pregnant woman with gestational diabetes(Ali & Kunugi, 2020).  
The most complete literature about the timing of food intake and duration of fasting during pregnancy is studies that evaluate Ramadan observance in pregnant Muslim populations. Although the characterization of participating in fasting differs by study, there is conflicting evidence about the impact on infant birth weight and maternal glycemia. Some studies identify greater risk of small-for-gestational age in infants whose parent fasted during gestation (Cross et al., 1990; Daley et al., 2017; Opaneye et al., 1990; Ziaee et al., 2010), or smaller birth weights(Savitri et al., 2014, 2018). The effect of fasting during pregnancy is less frequently studied, but demonstrates there may be small elevations in glycemia (Baynouna Al Ketbi et al., 2014). These data should be interpreted with caution, as the month of Ramadan not only results altered timing of eating, but also changes in sleeping patterns and dietary quality. Therefore, more research is warranted to disentangle the relationship between chrononutritional factors during pregnancy and perinatal health outcomes.

Because pregnancy is a critical period of development with opportunity to impact health of the pregnant person and their child and because evidence surrounding the timing of eating in these populations is minimal, we sought to examine the association between the timing of eating and duration of fasting and mid-gestation glycemia and birth weight in a pregnancy cohort. We hypothesized that those who have earlier meal timing and longer duration of overnight fast would have more favorable mid-gestation glucose tolerance test results without reductions in infant birth weights.

## Methods

### Study population

The Pregnancy Related Eating Sleeping, and Stress (PRESS) cohort was developed as a longitudinal, survey-based, clinical research study. This study was designed to understand nutritional and behavioral contributors to perinatal health. Participants were recruited into PRESS after being invited to enroll through email based on their status as a pregnant patient receiving care at Michigan Medicine between June 2022 and October2022 . Individuals who were interested in the study were directed toward a public REDCap link that results in a screening questionnaire. Those who were 18 years old, currently pregnant, in weeks 1-30 of pregnancy, and were currently receiving care and planning to deliver at Michigan Medicine we deemed as eligible and were invited to join the study.

Because individuals were eligible to join the study between 1-30 weeks of gestation, participants joined the study at various timepoints. Gestational age at enrollment was self-identified by answering the question, *“what week of your pregnancy are you currently in?”* which was verified in the medical chart upon enrollment. Survey information for analysis included those who participated at least once during the second trimester (14-28 weeks gestation, sent between 20-24 weeks) and third trimester (29-42+ weeks gestation, sent between 30-34 weeks). As participants could enroll in any trimester, they only received the surveys that were in line with target gestational weeks after enrollment. At the time of medical chart data abstraction in December 2022, the majority of participants that had delivered had only completed survey information for trimester 2 and trimester 3. Therefore, this analysis excludes data from trimester 1.

### Participant Exposures, Outcomes, and Covariates

The bulk of the survey instruments sent to participants were repeated for each data collection events. The detailed list of questionnaires sent for each trimester event is listed in figure 1.

with the exceptions being an additional sociodemographic and lifestyle factor questionnaire and anticipated gestational weight gain instrument in trimester 1 and question about most recent body weight in pounds and ounces in trimester 3.

#### Timing of first meal and last meal

The timing of eating during pregnancy was assessed during each trimester using a questionnaire that asked participants *“On a typical day during this trimester, when was the first time in the day you had something to eat? (This includes beverages that have calories; like coffee or tea with cream or sugar)”* to indicate the beginning of an eating window, and *“On a typical day during this trimester, when was the last you had something to eat before going to bed? (This includes beverages that have calories; like coffee with cream or sugar)”* to indicate the end of the eating window. We also collected timing of sleep onset and wake time. Participants provided answers to these questions with respect to both weekdays and weekends, for all eligible trimesters. Participants who did not report timing of eating or sleeping in military time were manually converted when necessary. Timing of eating data were inspected for overlap with reported sleeping intervals. Participant responses were evaluated for evidence of shift work, which was not apparent in the current sample.

#### Fasting duration and fasting midpoint

To determine fasting duration, we subtracted eating duration (the difference between the last eating occasion and first eating occasion, expressed hours and minutes) from 24 hours. The fasting midpoint was calculated as, time of last meal plus half the fasting duration.

#### Abstractions from medical chart data

Trained research staff accessed the participant’s medical charts to collect objective medical information about their current pregnancy. This included laboratory values, diagnoses of complications of pregnancy, parity, infant birth weight, sex of infant assigned at birth, and delivery method. Participants who did not have pre-existing diabetes underwent 1-hour oral glucose tolerance test (OGTT) during mid gestation (24-28 weeks’ gestation) according to Michigan Medicine guidelines. These labs were collected at a Michigan Medicine laboratory, where participants were instructed to consume a 50-gram liquid glucose drink in under 5 minutes. One hour later, blood was collected via venipuncture and glucose was determined by Michigan Medicine laboratory personnel. Primary outcomes of interest in this analysis were parent OGTT in mg/dL during mid-gestation and infant birth weight in grams.

#### Other Covariates

Sociodemographic and lifestyle information was collected upon enrolling in the study. This included data about self-reported pre-pregnancy BMI, physical activity, relationship status, smoking exposure, race/ethnicity, annual household income, and pregnant person’s level of education. Covariates were considered based on sociodemographic information available as well as *a priori* biological associations.

### Sensitivity analysis

After noticing attenuation of models for infant birth weight with adjustment for gestational age at delivery, we conducted a stratified analysis. We evaluated trimester 3 weekday exposures in relation to infant birth weight in the full sample and then again in a sample without individuals who delivered preterm. We selected stratified analysis as we were underpowered to complete a full mediation analysis.

### Statistical Analyses

Univariate analysis was completed on all sociodemographic, eating exposure, and health outcome data were assessed for normality through histograms and residual plots. Measures that are normally distributed are expressed as mean ± standard deviation (SD) and those that were not normally distributed are expressed as median ± inter-quartile range (IQR). After initial investigation of variables, we assessed the associations between covariates of interest and primary exposures and outcomes identified in this study, grouped by weekday or weekend and trimester. When data were distributed normally, association was determined through ANOVA. When data was not normally distributed, associations were assessed through Kruskal-Wallis test. Associations with a P-value <0.10 were considered as covariates for later trimester and weekday/weekend specific models. Due to low subject numbers in some categories of covariate groups, we collapsed them into fewer categories; such as dichotomizing self-reported race and ethnicity, parent educational attainment, annual household income. Final models for OGTT were adjusted for pre-pregnancy BMI, physical activity, sleep duration, annual household income, and dichotomized race/ethnicity. Infant birth weight models were adjusted for gestational age at birth, infant sex assigned at birth, sleep duration, annual household income, dichotomized race/ethnicity, and physical activity.

## Results:

### Timing of eating during pregnancy differs based on sociodemographic factors

While recruiting for this study, we excluded individuals with pre-existing diabetes, inaccurate or missing timing data, who were lost to follow up, those who delivered multiples, and those without outcome data at the time of the analysis. This resulted in 102 unique individuals, 54 who had survey responses for trimesters 2 and 3 (Figure 2). PRESS participants tended to be older (32.1 ± 0.54 years), highly educated (78.4% had at least one college degree), wealthy (63.7% >$100,000 a year), and had similar proportions of male and female infants (56.9% male).

In this population the timing of the first eating occasion on weekdays during the second trimester was associated with parent-reported race and ethnicity, maternal education, sleep duration, and marital status. Participants from historically excluded groups tended to eat their first and last meal later in the day, as well as have a later fasting midpoint (Tables 1). This was also true with respect to measures of socioeconomic status like household income and maternal education, where those who were wealthier and more highly educated tended to begin and finish eating earlier in the day than those with fewer resources. Participants who were married or in a partnership tended to consume meals earlier, begin fasts earlier and have earlier fating midpoints. Sleep duration greater than 8 hours was significantly associated timing of the first and last meal, as well as longer fasting durations, but not fasting midpoint. Similar associations were seen for weekend values during trimester 2. However, delivering before 37 weeks gestation was associated with later timing of first meal on weekend, and the timing of eating for both first and last meals tended to be later than on weekdays, although there were few individuals who delivered preterm (Table 2).

The timing of eating in trimester 3 on weekdays had fewer significant associations than did trimester 2 (Table 3). Later sleeping midpoint was associated with higher self-reported stress levels, which was driven by first meal. There were also more associations with gestational factors, such as earlier timing of first meal and vaginal delivery, and longer fasting duration occurring more in pregnancies that resulted in children assigned male sex at birth. Timing of eating variables in trimester 3 on weekends were also later than weekday, and with fewer associations (Table 4). Timing of first and last meal was again associated with parent race/ethnicity. Having greater amounts of physical activity during pregnancy was associated with lower oral glucose tolerance test in mid-gestation (Table 5). Whereas infant birth weight positively associated with gestational age at delivery.

### Infant birth weight is inversely associated with the timing of eating during pregnancy

Directionality of associations for birth weight with eating variables in trimester 2 were similar between weekdays and weekends. Generally, later eating times, and later fasting midpoint were associated with lower infant birth weights (Figure 3A). During the second trimester on weekends, each hour later initiation of the first meal was significantly associated a 125.28-gram reduction in infant birth weight (95% CI(-214.56, -36.00), p =0.0072 ). Later fasting midpoint was also associated with a 122.6-gram lower birth weight (95% CI(-230.0, -15.40), p =0.028). However, after adjustment for gestational age at delivery, both associations were attenuated, and remained similar with subsequent adjustment for infant sex, sleep duration, annual household income, race/ethnicity, and physical activity. There was no apparent relationship between fasting duration and infant birth weight during the second trimester.

The relationship between timing of eating and fasting variables were less consistent between weekdays and weekends in the third trimester. The timing of the last meal was positively associated with infant birthweight on weekdays (Figure 3B, 68.69 grams CI (1.64,138.96), p =0.0603), but negatively associated on weekends. Although neither of these associations were statistically significant. On weekdays in the third trimester, each hour later eating midpoint was related to a 104.7-gram lower in infant birth weight (Figure 3B, p=0.0001). This directionality was also observed for longer fasting durations were associated with 82.3 CI(-151.0, -55.1)-lower infant birth weights(p =0.022). Neither of these associations remained after adjustment for gestational age.

After observing that infant birth weight models were significantly attenuated in magnitude and significance by the addition of gestational age, we conducted a sensitivity analysis by stratifying data gestational age at delivery. We reanalyzed the same models in between those who delivered preterm vs full term. We employed stratified analysis because we had so few individuals with preterm deliveries in our sample (Tables 1 &3). In the full sample that included individuals who delivered preterm, longer fasting duration and later fasting midpoint was associated with significantly lower infant birthweights (Figure 3C; -82.3 CI(-151.0, -13.9) p=0.022 and -104.7 CI(-154.0, -55.1) p=0.0.00011, respectively). These associations were absent in the analysis that excluded individuals who delivered preterm.

### Later timing of eating is marginally related to parent glycemia in the second and third trimester

During the second trimester of pregnancy, the association between timing of eating variables and parent mid-gestation OGTT were comparable between weekdays and weekends. For each hour later timing of the first meal (Figure 3D), was related to a 5.14 mg/dL 95%CI(-0.09, 9.25) higher OGTT (p=0.058) which was not statistically significant. A similar association was seen for longer fasting duration being related to 3.71 mg/dL 95%CI(-0.019, 7.44) OGTT (p=0.055). However, after adjustment with covariates, these relationships no longer neared significance and were reduced in magnitude.

During the third trimester, timing of eating was more significantly related to OGTT values on weekdays than on weekends. For each hour the first meal of the weekday was delayed, there was a 6.67 mg/dL 95%CI(0.30, 13.07) greater 1-hour glucose value (Figure 3E, p=0.045). After adjustment for covariates, this association was fully attenuated.

## Discussion

In this study of 102 parent-child dyads, we found that later timing of the first meal on weekends during the second trimester was associated with a lower infant birth weights. There were also lower infant birthweights with later fasting midpoints and longer fasting duration during the third trimester. These associations failed to retain statistical significance after adjustment. Lower birthweights in relation to third trimester timing of first meal and fasting midpoint were driven by gestational age at delivery. To our knowledge, this is the first report in humans that finds later meal timing is associated with reduction in birth weight. As stated previously, there is a dearth of studies that evaluate timing of eating and duration of fasting in pregnancy outside of the literature describing observance of Ramadan fasting. Our findings are consistent with many studies of women fasting while pregnant during Ramadan. Reductions in birth weight were common, but they often failed to meet statistical significance(Savitri et al., 2014, 2018; Ziaee et al., 2010). Rates of low-birthweight or small for gestational age have also found to be increased in pregnant women observing Ramadan (Cross et al., 1990; Daley et al., 2017; Opaneye et al., 1990; Ziaee et al., 2010). Although we did not evaluate this outcome, it should be considered as a future direction.

Of importance, we discovered that the association between timing of eating during the third trimester and infant birth weight was specific to populations that included preterm births. There have been studies that have linked chronobiological behaviors to risks of preterm birth, but these studies focused on sleep (Martin-Fairey et al., 2019) or the relationship between shortened sleep and eating during the night (Loy et al., 2020). Although we included measurements of sleep duration in our fully adjusted models for birth weight, we did so using a self-report measure that doesn’t include sleep quality, architecture, or disturbances. It is possible that changes in sleep could underlie part of this association seen in our study, but we are limited by instrumentation error inherent in our measurement. Further independent examinations of the relationship between chronobiological behaviors, including eating and sleeping, should be conducted with respect for infant size for gestational age. This study had fewer than 10 individuals (<10% of the sample) that delivered preterm, so we were underpowered to examine this association any further.

The associations we found between the timing of eating during trimester 2 or 3 and parent oral glucose tolerance test in mid-gestation were small in magnitude and failed to reach statistical significance after adjustment with covariates. Based on our sample size and R-squared value for detecting changes in OGTT from fasting duration in tri 3 on weekdays, we only achieved 68% power. This suggests that with a larger sample, we would have been more able to detect significant associations. Despite our more limited sample size, our findings are in line with another study in 1061 pregnancy people in the GUSTO cohort that demonstrated that longer duration of overnight fast and additional meal frequency was positively related to a small (0.03mg/dL), but statistically significant increase in fasting glucose (Loy et al., 2017). In relation to Ramadan, maternal glycemia was increased by observing fasting during pregnancy (Baynouna Al Ketbi et al., 2014), increased HOMA-IR (Ajabnoor et al., 2014). The mechanism for the associations in unknown, although there is evidence that there is blunting of the cortisol diurnal rhythm (Bahijri et al., 2013) in pregnant populations who fast for Ramadan. As the fasting period is also paired with chronodisruption and sleep changes, it is difficult to compare this finding to the current study. There is also the concern that the strongest relationship with mid-gestation glycemia occurs in trimester 3, which is after the timing of the OGTT. This may be explained by reverse causality in those who had been diagnosed with gestational diabetes. This is because all patients who are diagnosed with GDM are referred to a dietitian and a diabetes educator, which would result in implementation of lifestyle changes including dietary quality and even pharmacological management. Although we had low rates of GDM in our sample (12 cases total). It is also likely that dietary quality as an independent factor or in relation with timing of eating drove much of the association. This makes sense since earlier eating times has been shown to be associated with better dietary quality in pregnant populations(Gontijo et al., 2020). Taken together, the data suggest that lengthening the duration of the fast or manipulating timing of eating this may not be a suitable dietary regimen in pregnant populations that are at risk for low-birth-weight infants or GDM.

The current study was impacted by several limitations. First, the sample size was relatively small, and few participants had repeated measurements, affecting our statistical power to detect associations in our outcomes, especially after adjustment for relevant covariates. There is also the possibility that residual confounding remains in our assessments, either based on measurement and instrumentation error, or effects from covariates that were not collected. The results are also difficult to generalize, as the PRESS cohort is not a racially, ethnically, or economically diverse population. Generalization to other pregnant people should be limited to populations that are similar in sociodemographic and lifestyle. There is likely an effect of these lived experiences on the timing of eating that we did not capture with our instruments, which is apparent based on strong bivariate associations.

This study had several strengths that distinguish it from other studies assessing the timing of eating in pregnant populations. The exposures analyzed in the current work included multiple trimesters, which allows detect distinct associations during specific periods of fetal development. We also evaluated weekday and weekend responses separately, as evidence from NHANES suggests that diet vary significantly in timing and quality between the two (An, 2016). The lack of shift work evident in responses also make assessing the relationship between timing of eating and perinatal health outcomes more straightforward than if there had been shift workers.

## Conclusions

Later timing of eating during the second and third trimester of pregnancy may result in lower infant birth weights. Longer fasting durations and later meal timing may also be related to a modest increase in mid gestation OGTT. As such, timing of eating and duration of overnight fasts should be considered as both an area of further research and a factor to consider when counseling patients navigating pregnancy. These current study must be replicated in a more diverse and larger population to confirm these associations before formal recommendations can be made for clinical practitioners seeking to modulate circadian health of pregnant populations.

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