

Maternal lipid levels during pregnancy and child weight status at 3 years of age

Chantel L. Martin¹  | Catherine J. Vladutiu^{2,3}  | Tarek M. Zikry⁴ | Matthew R. Grace⁵ | Anna Maria Siega-Riz⁶

¹Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina

²Department of Obstetrics & Gynecology, University of North Carolina School of Medicine, Chapel Hill, North Carolina

³Maternal and Child Health Bureau, Health Resources and Services Administration, Rockville, Maryland

⁴Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina

⁵Department of Obstetrics and Gynecology, University of Tennessee Health Sciences Center College of Medicine, Nashville, Tennessee

⁶School of Nursing and Departments of Public Health Sciences and Obstetrics & Gynecology School of Medicine, University of Virginia, Charlottesville, Virginia

Correspondence

Chantel L. Martin, Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC 27599.

E-mail: chantelmartin@unc.edu

Funding information

National Institutes of Health, Grant/Award Numbers: HD-28684, HD-28684A, HD-375874, HD-39373, Research Center R24 HD-050924, T32CA128582 and T32ES007018; National Institute of Environmental Health Sciences, Grant/Award Number: T32ES007018; National Cancer Institute, Grant/Award Number: T32CA128582; Eunice Kennedy Shriver National Institute of Child Health and Human Development, Grant/Award Numbers: R24HD050924, HD-39373, HD-375874, HD-28684A and HD-28684

1 | INTRODUCTION

Childhood obesity is increasingly common in the United States (U.S.), affecting approximately 8.9% of U.S. children ages 2 to 5 years.¹

Abbreviations: BMI, body mass index; CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; MET, metabolic equivalent; PIN, Pregnancy, Infection, and Nutrition; RR, risk ratio; SD, standard deviation

Summary

Background: The intrauterine environment is critical in the development of child obesity.

Objective: To investigate the association between maternal lipid levels during pregnancy and child weight status.

Methods: Maternal lipid levels (total cholesterol, high-density and low-density lipoprotein cholesterol, triglycerides) collected from fasting blood samples collected at less than 20 and 24–29 weeks' gestation and child weight status at age 3 were examined prospectively among 183 mother-child dyads enrolled in the Pregnancy, Infection, and Nutrition. Measured height and weight at 3 years were used to calculate age- and sex-specific body mass index z-scores. Child risk of overweight/obesity was defined as body mass index greater than or equal to 85th percentile for age and sex. Regression models estimated the association between maternal lipid levels and child body mass index z-score and risk of being affected by overweight/obesity, respectively.

Results: Higher triglyceride levels at less than 20 and 24–29 weeks of pregnancy were associated with higher body mass index z-scores ($\beta = 0.23$; 95% CI: 0.07–0.38 and $\beta = 0.15$; 95% CI: 0.01–0.29; respectively) after adjusting for confounders. There was no evidence of an association between total or low-density lipoprotein cholesterol and child weight status at age 3.

Conclusions: Early childhood body mass index may be influenced by maternal triglyceride levels during pregnancy.

KEYWORDS

child obesity, cholesterol, pregnancy, triglycerides

Children affected by overweight or obesity are at increased risk of adverse health outcomes, including high blood pressure and cholesterol, asthma, type II diabetes, and several other chronic physiologic and psychosocial health conditions.² Childhood obesity is also a strong predictor of obesity in later life and children who have obesity are at greater risk of developing adverse health conditions in adulthood.²

Intrauterine exposures influence the health of children, and perinatal maternal health status is recognized as an important risk factor for childhood obesity.³ Previous research suggests that maternal lipid profiles during pregnancy may provide an additional source of energy to the foetus, potentially influencing foetal adiposity and growth.⁴ Prior studies have examined associations between maternal lipids and child anthropometric outcomes beyond birth,⁴⁻⁶ yet they are limited by nonfasting exposure measures⁵ and measures of lipids at only one time point in pregnancy.^{5,6}

Understanding the impact of maternal lipid profiles on child weight status beyond infancy is important for informing efforts to optimize foetal health and subsequently decrease the prevalence of obesity and corresponding life course trajectories in children. The objective of our study was to examine the association between maternal lipid levels during two time points in pregnancy and weight status at 3 years of age among a cohort of North Carolina mother-child pairs enrolled in the Pregnancy, Infection, and Nutrition (PIN) study. We hypothesized that women with higher lipid concentrations during pregnancy would have children with higher body mass index (BMI) z-scores and greater risk of overweight or obesity.

2 | METHODS

2.1 | Study design and sample

This analysis included data from pregnant women participating in the third cohort of the PIN prenatal study with follow-up of children through 3 years post-partum by the PIN PIN Postpartum (3 and 12 mo) and PIN Kids (3 y post-partum) studies. Details of the study protocols have been published previously.^{7,8} In brief, pregnant women who were less than 20-weeks' gestation, English-speaking, more than or equal to 16 years of age, and planning to continue prenatal care were recruited from University of North Carolina prenatal clinics to participate in the prenatal study from 2001 to 2005. Participants were asked to complete two research clinic visits (one at <20-weeks' gestation and one at 24-29-weeks' gestation) and two telephone interviews (one at 17-22-weeks' gestation and a second at 27-30-weeks' gestation). Self-administered questionnaires were also collected at the two research clinic visits. All PIN study protocols were reviewed and approved by the Institutional Review Board of the UNC School of Medicine.

A total of 1169 pregnant women in PIN who delivered a live singleton birth were eligible for recruitment into the post-partum study. Of those eligible, 689 (at 3 mo post-partum) and 550 (at 12 months post-partum) mother-child pairs participated. The most common reasons for non-participation were refusal/request to leave the study ($n = 202$), unreachable/moved out of study catchment area ($n = 226$), and ineligibility because of medical reasons, timing issues, or becoming pregnant again ($n = 338$). Recruitment for PIN Kids, an assessment of the index child at 3 years of age, began in 2004. A total of 409 mother-child pairs consented and participated in this 3-year follow-up out of the 550 who completed the 12-month visit. Children with missing anthropometric measurements ($n = 81$) or those who had a physician-diagnosed illness related to growth ($n = 3$) were not included in these analyses. Furthermore, 107 mothers were missing lipid

biomarker values at both time points, 26 had pre-existing diabetes and/or hypertension, three had multiple pregnancies during the PIN prenatal study, and six were missing information on gestational age at blood draw, weight gain during pregnancy, or self-reported race. The final sample included 183 mother-child pairs. We compared baseline maternal and child characteristics of eligible mother-child pairs who participated at the 3-year visit but were excluded from our analysis ($n = 226$), with those remaining in our analytic sample ($n = 183$) and found no significant differences.

2.2 | Measures

2.2.1 | Outcome variable: Child weight status

All height and weight measurements were collected by trained PIN study staff during the 3-year home visit. Children's standing heights and weights were measured using stadiometers and scales according to the National Health and Nutrition Examination Survey protocols (CDC/NCHS, NHANES protocol 1999-2000). Children were, on average, 3.0 ± 0.2 years of age at the home visit. Age- and sex-specific BMI z-scores and percentiles were calculated from the measured heights and weights using the 2000 Centres for Disease Control and Prevention growth charts for children greater than or equal to 24 months.⁹ Children were classified as being affected by overweight or obesity if BMI-for-age and sex were greater than or equal to 85th percentile. Offspring weight status was examined according to risk of obesity using the dichotomous specification (BMI-for-age and sex ≥ 85 th percentile) and to identify the linear association in relation to maternal lipid levels using the continuous specification (BMI z-score).

2.2.2 | Exposure variables: Maternal lipid levels

Fasting blood samples were collected at two time points during pregnancy: less than 20-weeks' gestation and 24-29-weeks' gestation. Maternal lipid levels, including triglycerides (mg/dL), cholesterol (mg/dL), high-density lipoprotein (HDL) cholesterol (mg/dL), and low-density lipoprotein (LDL) cholesterol (mg/dL), were assayed by LipoScience, Inc (now Laboratory Corporation of America, Burlington, NC USA) using nuclear magnetic resonance technique (NMR LipoProfile-II autoanalyser, Liposcience Inc.).

2.2.3 | Covariates

Maternal age, race, education, income, and household size (used to calculate percentage of the 2001 federal poverty level¹⁰), parity, and marital status were self-reported during the first telephone interview; smoking in the first 6 months of pregnancy was reported in the second phone interview. Interviewers administered a 7-day recall questionnaire on physical activity during the telephone interview at 17-22-weeks' gestation.¹¹ Frequency and duration was assessed for all moderate and vigorous occupational, recreational, household, child and adult care, and transportation activities. Using the Borg scale, perceived intensity was estimated and total metabolic equivalent (MET) hours in the past week (MET h/week) were calculated.^{12,13} Maternal prepregnancy BMI was calculated from self-reported prepregnancy weight and measured

height and categorized according to the Institute of Medicine's (2009) recommendations.¹⁴ Missing or implausible prepregnancy weights were imputed for 2.7% of our study population with the use of measured weight at the first prenatal care visit. Maternal trimester-specific weight was estimated using the rate of weight gain. This rate was calculated by subtracting the participant's self-reported prepregnancy weight from her weight as measured at the study visit and dividing by the number of weeks' gestation. The rate of weight gain was then multiplied by 13 weeks to obtain the total first trimester weight and by 26 weeks to obtain maternal weight at the end of the second trimester. Gestational diabetes and pregnancy-induced hypertension for the pregnancy were ascertained through a review of prenatal records. Information on gestational age at birth and child birth weight was available from delivery records. At the 3-year home visit, women were asked to recollect the age at which they stopped breastfeeding, which was converted to breastfeeding duration in weeks.

2.3 | Statistical analysis

We conducted descriptive analyses to examine maternal and infant characteristics and to assess the distribution of lipid levels at less than 20 and 24-29-weeks' gestation. Linear regression models were used to estimate the association between maternal lipids, scaled to one standard deviation (1-SD), and child BMI z-score at 3 years of age. Binomial regression models with robust standard errors were used to estimate risk ratios (RR) and 95% confidence intervals (CI) for the association between maternal lipids and child overweight/obesity. Separate models were examined for each lipid (total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol) at <20 and 24-29 weeks' gestation and the change across the two time points. Potential confounding factors were identified a priori from the literature and included in the model based on the directed acyclic graph (DAG).¹⁵ Variables are considered confounding factors according to the DAG if they are believed to have a causal association with the exposure and outcome and do not lie along the causal pathway. Variables included across models were gestational age at blood draw, first trimester weight gain (for 20-weeks' analysis only), second trimester weight gain (for 24-29-weeks' analysis only), maternal age, pregnancy-induced hypertension, gestational diabetes, and smoking. We also considered effect measure modification by prepregnancy BMI. Analyses were performed using SAS 9.3 software (SAS Institute, Cary, NC).

3 | RESULTS

Table 1 provides selected baseline characteristics of the study population. The majority of women were white (89.6%), college educated (86.4%), from high-income households (>350% of the federal poverty level; 64.5%), married (88.0%), and non-smokers during pregnancy (91.8%). The mean \pm SD age and prepregnancy BMI were approximately 29.7 \pm 5.3 years and 25.1 \pm 6.5 kg/m², respectively. Approximately, 34.4% of the women were categorized as being affected by overweight (19.1%) or obesity (15.3%) prior to pregnancy. On average, children were delivered at 39-weeks' gestation, weighed nearly 3400 \pm 678 grams at birth, and were breastfed for approximately

TABLE 1 Selected characteristics of mother-child pairs included in the study population, Pregnancy, Infection, and Nutrition (*n* = 183)

	Mean \pm SD or <i>n</i> (%)
Maternal characteristics	
Age, years	29.7 \pm 5.3
Race	
White	164 (89.6)
Non-White	19 (10.4)
Education, years	
Grade \leq 12	25 (13.4)
Grade 13-16	94 (51.4)
Grade \geq 17	64 (35.0)
Household income, % federal poverty level	
<185%	28 (15.3)
185-350%	37 (20.2)
>350%	118 (64.5)
% Married	161 (88.0)
% Nulliparous	91 (49.7)
% Smoked in first 6 months	15 (8.2)
Prepregnancy BMI, kg/m ²	25.1 \pm 6.5
Prepregnancy BMI category	
Underweight, <18.5 kg/m ²	10 (5.5)
Normal weight, 18.5-24.9 kg/m ²	110 (60.1)
Overweight, 25.0-29.9 kg/m ²	35 (19.1)
Obese, \geq 30.0 kg/m ²	28 (15.3)
Gestational age at <20 weeks blood draw, weeks	18.1 \pm 1.5
Gestational age at 24-28 weeks blood draw, weeks	27.5 \pm 1.4
Estimated weight gain by end of 1 st trimester, pounds	4.7 \pm 6.4
Estimated weight gain by end of 2 nd trimester, pounds	20.5 \pm 9.8
% Gestational Diabetes diagnosis	6 (3.3)
% Pregnancy-induced hypertension	12 (6.6)
Physical activity level at <20 weeks' gestation, MET h/week	27.2 \pm 28.6
Childhood characteristics	
Gestational age at delivery, weeks	38.9 \pm 1.6
% Male	100 (54.6)
Birth weight, grams	3389.8 \pm 677.9
BMI z-score at 3 years of age	0.27 \pm 1.0
Breastfeeding duration in weeks	35.4 \pm 25.9
% affected by overweight/obesity	35 (19.1)

Abbreviations: BMI, body mass index; MET, metabolic equivalent

35.4 \pm 25.9 weeks (8.1 \pm 6.0 months). At 3 years of age, 19.1% of children were classified as being affected by overweight/obesity.

Table 2 presents mean \pm SD maternal lipid levels at less than 20-weeks' gestation and 24-29-weeks' gestation by child weight outcomes at 3 years of age (BMI <85th percentile and BMI \geq 85th percentile) and the average change across the two periods. On average, the change in total cholesterol, triglyceride, and LDL cholesterol levels from less than 20 weeks to 24-29 weeks was greater among children

TABLE 2 Mean and standard deviation of maternal lipids during pregnancy and child weight outcomes at 3 years of age. Pregnancy, Infection, and Nutrition (n = 183).

	Non-overweight/obese (BMI <85th percentile) n = 148			Overweight/Obese (BMI ≥85th percentile) n = 35		
	<20 weeks Mean (SD)	24–29 weeks Mean (SD)	Mean Change (SD)	<20 weeks Mean (SD)	24–29 weeks Mean (SD)	Mean Change (SD)
Total Cholesterol, mg/dL	203.5 (34.3)	251.2 (43.0)	48.5 (26.4)	200.3 (41.4)	242.9 (50.3)	42.3 (31.8)
Triglycerides, mg/dL	121.5 (54.2)	170.2 (62.7)	48.8 (43.1)	148.4 (54.2) ^A	191.9 (76.0) ^B	41.6 (52.5)
HDL cholesterol, mg/dL	59.7 (11.6)	61.8 (12.5)	2.1 (7.7)	55.4 (14.1) ^B	58.4 (13.1)	3.8 (11.6)
LDL cholesterol, mg/dL	123.3 (29.4)	158.7 (39.5)	35.7 (23.1)	123.9 (36.1)	152.8 (45.0)	27.9 (27.4)

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.

^ADifferent from non-overweight/obese group at same time point, P value < 0.05

^BDifferent from non-overweight/obese group at same time point, P value < 0.10

with BMI less than 85th percentile than children affected by overweight/obesity. We also observed slightly lower change in mean HDL cholesterol levels among children with BMI less than 85th percentile when compared with those affected by overweight/obesity across the two periods.

0.15-unit increase in children BMI z-score at 3 years of age (95% CI: 0.01, 0.29), after adjusting for confounders (Model 2). We did not observe any associations between the change in maternal lipid levels from less than 20 weeks to 24-29 weeks and BMI z-score.

3.1 | Child BMI z-score

Table 3 presents associations of maternal lipid levels at less than 20-weeks' gestation, 24-29-weeks' gestation, and across the two time periods with child BMI z-score at 3 years of age. At less than 20-weeks' gestation, a 1-SD increase in triglycerides was associated with higher BMI z-scores at 3 years (regression coefficient: 0.26; 95% CI: 0.12, 0.40), after adjusting for gestational age at blood draw (Model 1). Further, HDL-cholesterol was inversely associated with child BMI z-score, such that a 1-SD increase in HDL-cholesterol was associated with lower BMI z-scores (regression coefficient: -0.18; 95% CI: -0.32, -0.03). Additional adjustment for trimester-specific weight gain, maternal age, diagnosis of pregnancy-induced hypertension or gestational diabetes, smoking in the first 6 months of pregnancy, and prepregnancy BMI attenuated the results (Model 2). Triglyceride levels remained positively associated with child BMI z-score (regression coefficient = 0.23; 95% CI: 0.07, 0.38).

At 24-29-weeks' gestation, a similar positive association was observed between maternal triglyceride levels and child BMI z-score (Table 3). A 1-SD increase in triglycerides was associated with a

3.2 | Child overweight/obesity

At less than 20-weeks' gestation and 24-29-weeks' gestation, a 1-SD increase in maternal triglycerides was associated with a higher risk of having a child affected by overweight/obesity at 3 years of age as opposed to having a child classified as not being affected by overweight/obesity (RR = 1.28, 95% CI: 1.02, 1.59), after adjusting for gestational age at blood draw (Table 4). This association was attenuated at both time points after adjusting for additional confounding factors. There was no evidence of an association between the change in maternal lipid levels across both time points during pregnancy and child overweight/obesity.

4 | DISCUSSION

In this sample of mother-child pairs, we examined measures of maternal total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol at less than 20-weeks' gestation and 24-29-weeks' gestation in relation to child weight measurements at 3 years of age. At less than 20-weeks' gestation, we found that higher maternal triglyceride levels and lower HDL-cholesterol levels were associated with higher

TABLE 3 Maternal lipids during pregnancy and child BMI z-score at 3 years of age, Pregnancy, Infection, and Nutrition study (n = 183)

	<20-weeks' gestation		24-29-weeks' gestation		Change from <20-weeks' gestation to 24-29-weeks' gestation	
	Model 1 ^a β (95% CI)	Model 2 ^b β (95% CI)	Model 1 ^a β (95% CI)	Model 2 ^b β (95% CI)	Model 1 ^a β (95% CI)	Model 2 ^b β (95% CI)
Total Cholesterol, mg/dL	0.01 (-0.15, 0.16)	0.00 (-0.15, 0.15)	0.00 (-0.15, 0.14)	0.03 (-0.12, 0.18)	-0.02 (-0.17, 0.13)	0.04 (-0.11, 0.19)
Triglycerides, mg/dL	0.26 (0.12, 0.40)	0.23 (0.07, 0.38)	0.16 (0.02, 0.31)	0.15 (0.01, 0.29)	-0.07 (-0.22, 0.08)	-0.05 (-0.20, 0.10)
HDL cholesterol, mg/dL	-0.18 (-0.32, -0.03)	-0.12 (-0.27, 0.02)	-0.08 (-0.23, 0.06)	-0.06 (-0.20, 0.09)	0.11 (-0.05, 0.27)	0.10 (-0.05, 0.25)
LDL cholesterol, mg/dL	0.06 (-0.09, 0.21)	0.04 (-0.11, 0.18)	0.00 (-0.15, 0.15)	0.04 (-0.11, 0.19)	-0.11 (-0.26, 0.05)	-0.03 (-0.18, 0.13)

Abbreviations: BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

^aModel 1 is adjusted for gestational age at blood draw.

^bModel 2 is adjusted for gestational age at blood draw, weight gained in first trimester (second trimester for Time 2), maternal age, pregnancy-induced hypertension, gestational diabetes, smoking, and prepregnancy body mass index.

TABLE 4 Maternal lipids during pregnancy and child risk of overweight/obesity (BMI \geq 85th percentile) at 3 years of age, Pregnancy, Infection, and Nutrition (n = 183)

	<20-weeks' gestation		24-29-weeks' gestation		Change from <20-weeks' gestation to 24-29-weeks' gestation	
	Model 1 ^a RR (95% CI)	Model 2 ^b RR (95% CI)	Model 1 ^a RR (95% CI)	Model 2 ^b RR (95% CI)	Model 1 ^a RR (95% CI)	Model 2 ^b RR (95% CI)
Total Cholesterol, mg/dL	0.90 (0.65, 1.24)	0.95 (0.69, 1.30)	0.85 (0.62, 1.15)	0.89 (0.63, 1.24)	0.83 (0.59, 1.15)	0.88 (0.64, 1.20)
Triglycerides, mg/dL	1.28 (1.02, 1.59)	1.22 (0.90, 1.65)	1.28 (1.02, 1.59)	1.21 (0.94, 1.55)	0.98 (0.73, 1.31)	0.91 (0.69, 1.20)
HDL cholesterol, mg/dL	0.72 (0.49, 1.06)	0.89 (0.63, 1.26)	0.80 (0.58, 1.11)	0.85 (0.63, 1.17)	1.15 (0.94, 1.40)	1.12 (0.90, 1.40)
LDL cholesterol, mg/dL	0.98 (0.72, 1.34)	0.98 (0.73, 1.31)	0.87 (0.64, 1.19)	0.90 (0.64, 1.25)	0.75 (0.54, 1.03)	0.81 (0.58, 1.13)

Abbreviations: BMI, body mass index; RR, risk ratio; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

^aModel 1 is adjusted for gestational age at blood draw.

^bModel 2 is adjusted for gestational age at blood draw, weight gained in first trimester (second trimester for Time 2), maternal age, pregnancy-induced hypertension, gestational diabetes, smoking, and prepregnancy body mass index

BMI z-scores at 3 years of age. Evidence of a positive association between maternal triglycerides and BMI z-scores remained after adjustment for potential confounding factors. Similar patterns of associations between maternal triglyceride levels and BMI z-scores were observed at 24-29-weeks' gestation. When child BMI percentile was dichotomized as less than 85th percentile and greater than or equal to 85th percentile, there was evidence of an increased risk of being affected by overweight/obesity for every 1-SD increase in maternal triglycerides levels at less than 20-weeks' gestation and 24-29-weeks' gestation after adjusting for gestational age at blood draw. These findings are important, especially considering our study sample of mostly White and highly educated mothers. Children with these sociodemographic characteristics are often considered at lower risk of being affected by overweight/obesity; however, our results support an association with increased BMI z-score and higher risk of overweight/obesity.

Previous studies on maternal lipid levels during pregnancy and early childhood weight status are limited. To our knowledge, only three prior studies have investigated the association between maternal lipid levels during pregnancy and child adiposity,⁴⁻⁶ and the results are mixed. Similar to our study, Gademen et al observed evidence of positive associations between maternal triglyceride levels during pregnancy (mean: 13-weeks' gestation) and child waist-to-hip ratio at 5-6 years of age. Like our study, Geraghty et al. examined multiple measures of fasting blood lipids (during pregnancy at ~14- and ~28 weeks' gestation, and at delivery in cord blood) in relation to child anthropometric measurements at birth, 6 months, and 2 years of age. Maternal triglyceride levels at approximately 28-weeks' gestation were positively associated with birthweight, while cord triglyceride levels were inversely associated with birth weight. However, no association was observed between maternal triglycerides and early childhood weight. Similarly, Daraki et al. did not report an association between maternal triglyceride levels collected during early pregnancy (mean: 12-weeks' gestation) and anthropometric measures at 4 years of age. Methodological differences, such as differences in blood sample collections, variations in timing and frequency of lipid measurements, and differences in timing of child weight measurements, may contribute to these inconsistent findings.

Studies have also examined the association of maternal lipids with early life (neonatal and infant) weight outcomes.

The Healthy Start Study examined the association between maternal fasting metabolic fuels (ie, glucose, insulin resistance [HOMA-IR], total cholesterol, HDL-cholesterol, triglycerides, and free fatty acids) at less than 20-weeks' and greater than or equal to 20-weeks' gestation and neonatal body composition collected from PEA POD measurements.¹⁶ No association was found with triglycerides; however, the authors identified an inverse association between HDL-cholesterol and neonatal fat mass and fat mass percent,¹⁷ which is in line with our finding that HDL-cholesterol at less than 20-weeks' gestation was associated with lower BMI z-score at 3 years of age when adjusted for gestational age at blood draw. Furthermore, Vrijkotte et al (2015) reported a positive association between triglycerides and birth weight and infant anthropometric measurements, yet the study did not include fasting blood samples, which makes it difficult to make comparisons across the studies.¹⁸

4.1 | Biological mechanisms

There are several mechanisms that may explain the association between maternal lipid levels and early childhood weight status. The maternal overnutrition hypothesis postulates that maternal lipid metabolism may influence childhood adiposity through altered appetite and regulation and adipocyte metabolism.¹⁸ Compelling experimental research shows that a high-fat diet during pregnancy can lead to dysregulation of the hypothalamus, an important regulator of lipid metabolism and satiety, which may alter the dietary habits and patterns of children.^{19,20} A recent study of pregnant women in the PIN cohort found evidence of an association between diet quality during pregnancy and maternal triglyceride levels at 26-29-weeks' gestation.²¹ Additional research is warranted to investigate whether children exposed to high-fat/low quality diets during pregnancy have poor eating behaviours during childhood compared with unexposed children. Mothers and children share postnatal environments during early life. Shared behavioural patterns, such as dietary intake and physical inactivity, between the mother and child could contribute to an increased risk of child obesity. It is also possible that genetic and epigenetic factors may help to explain the effects of maternal lipid metabolism on childhood adiposity, as placental lipoprotein lipase, responsible for placental lipid transfer, and DNA methylation were

associated with cord blood lipids.²² Further research is needed to disentangle the complex mechanistic pathways between maternal lipid metabolism and child adiposity.

4.2 | Strengths and limitations

This study builds on the existing literature by examining the association between maternal lipid levels and child weight at 3 years using fasting blood samples collected at two time points in pregnancy. Additional strengths of this study include the prospective cohort design, access to medical records, information on several potential covariates, and measured weight and height for children. Due to the prospective design and repeated collection of information at two time points, we were able to examine longitudinal associations between the change in lipid levels and child weight status.

There are several limitations to consider when interpreting our results. First, BMI is a proxy for adiposity and does not distinguish between body fatness, muscle mass, and skeletal mass. Despite this limitation, studies have shown that the CDC BMI-for-age percentiles are good indicators for identifying children with excess body fat.²³ Information on selected covariates was self-reported (eg, prepregnancy weight and smoking) and are subject to misclassification from recall. There may also be confounding by factors that were unmeasured in this study. While the number of overweight/obese children reflects a small sample, the proportion is relatively high (19%), particularly for children with demographic characteristics often noted at lower risk of overweight/obesity (eg, White race and high parental education levels). The generalizability of this study may be limited, as the women were recruited from one clinic in central North Carolina and likely do not represent the general population. Further, the women in our sample were not representative due to attrition and exclusion criteria, which resulted in a homogenous study sample of majority White and highly educated women. This likely resulted in an underestimation of the associations between maternal lipids and offspring weight status.

5 | CONCLUSIONS

Despite the study limitations, the results from our study suggest that an intrauterine environment characterized by increasing triglycerides during pregnancy influences weight status in early childhood. Specifically, we found that children of mothers with higher triglyceride levels during early (<20-weeks' gestation) and mid- (24-29-weeks' gestation) pregnancy had higher BMI z-scores and are at greater risk of overweight/obesity at 3 years of age. The findings of our study underscore the need for additional research among larger, more racially and socially diverse populations to better understand the influence of maternal lipid levels on the risk of childhood obesity.

ACKNOWLEDGEMENTS

AMSR, CM, and CV conceived and planned this secondary analysis. The analysis of the data was performed by CM and TZ. The manuscript was written by CM and CV, with revisions and final approval from AMSR, MG, and TZ. The Pregnancy, Infection and Nutrition

Study is a joint effort of many investigators and staff members, whose work is gratefully acknowledged. This study was funded in part by NIH grants HD-28684, HD-28684A, HD-375874, HD-39373, R24HD050924, and NIH Training Grants from National Cancer Institute (T32CA128582) and National Institute of Environmental Health Sciences (T32ES007018).

CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

DISCLAIMER

The views expressed in this publication are solely the opinions of the authors and do not necessarily reflect the official policies of the U.S. Department of Health and Human Services and the Health Resources and Services Administration, nor does mention of the department or agency names imply endorsement by the U.S. Government.

ORCID

Chantel L. Martin  <http://orcid.org/0000-0003-1907-0810>

Catherine J. Vladutiu  <http://orcid.org/0000-0002-8840-2199>

REFERENCES

1. Ogden CL, Carroll MD, Lawman HG, *et al.* Trends in obesity prevalence among children and adolescents in the United States, 1988-1994 Through 2013-2014. *JAMA* 2016; 315: 2292-2299.
2. Centers for Disease Control and Prevention. Childhood obesity causes & consequences. 2018. [WWW document] URL <https://www.cdc.gov/obesity/childhood/causes.html>.
3. Oken E. Maternal and child obesity: the causal link. *Obstet Gynecol Clin N Amer* 2009; 36: 361-377 ix-x.
4. Geraghty AA, Alberdi G, O'Sullivan EJ, *et al.* Maternal blood lipid profile during pregnancy and associations with child adiposity: findings from the ROLO study. *PLoS One* 2016; 11: e0161206.
5. Gademan MG, Vermeulen M, Oostvogels AJ, *et al.* Maternal prepregnancy BMI and lipid profile during early pregnancy are independently associated with offspring's body composition at age 5-6 years: the ABCD study. *PLoS One* 2014; 9: e94594.
6. Daraki V, Georgiou V, Papavasiliou S, *et al.* Metabolic profile in early pregnancy is associated with offspring adiposity at 4 years of age: the Rhea pregnancy cohort Crete, Greece. *PLoS One* 2015; 10: e0126327.
7. Mehta UJ, Siega-Riz AM, Herring AH. Effect of body image on pregnancy weight gain. *Matern Child Health J* 2011; 15: 324-332.
8. Deierlein AL, Siega-Riz AM, Herring AH, Adair LS, Daniels JL. Gestational weight gain and predicted changes in offspring anthropometrics between early infancy and 3 years. *Pediatr Obes* 2012; 7: 134-142.
9. Kuczumski RJ, Ogden CL, Guo SS, *et al.* CDC growth charts for the United States: methods and development. *Vital Health Stat* 2000; 2002: 1-190.
10. Proctor B, Dalaker J. U.S. Bureau of the Census, Current Population Reports, Series P60-219, Poverty In the United States: 2001. Washington, DC; 2002.
11. Borodulin K, Evenson K, Wen F, Herring A, Benson A. Physical activity patterns during pregnancy. *Med Sci Sports Exerc* 2008; 40: 1901-1908.
12. Ainsworth B, Haskell W, Leon AS, *et al.* Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993; 25: 71-80.

13. Ainsworth BE, Haskell WL, Whitt MC, *et al.* Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 2000; 32: S498–S504.
14. Institute of Medicine. *Weight Gain During Pregnancy: Reexamining the Guidelines*. The National Academies Press: Washington, DC, 2009.
15. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiological research. *Epidemiology* 1999; 10: 37–48.
16. Crume TL, Shapiro AL, Brinton JT, *et al.* Maternal fuels and metabolic measures during pregnancy and neonatal body composition: the healthy start study. *J Clin Endocrinol Metab* 2015; 100: 1672–1680.
17. Vrijkotte TG, Algra SJ, Brouwer IA, van Eijsden M, Twickler MB. Maternal triglyceride levels during early pregnancy are associated with birth weight and postnatal growth. *J Pediatr* 2011; 159: 736–742.e1.
18. McMillen IC, Edwards LJ, Duffield J, Muhlhausler BS. Regulation of leptin synthesis and secretion before birth: implications for the early programming of adult obesity. *Reproduction* 2006; 131: 415–427.
19. Chang GQ, Gaysinskaya V, Karatayev O, Leibowitz SF. Maternal high-fat diet and fetal programming: increased proliferation of hypothalamic peptide-producing neurons that increase risk for overeating and obesity. *J Neurosci* 2008; 28: 12107–12119.
20. Chen H, Simar D, Lambert K, Mercier J, Morris MJ. Maternal and post-natal overnutrition differentially impact appetite regulators and fuel metabolism. *Endocrinology* 2008; 149: 5348–5356.
21. Martin CL, Siega-Riz AM, Sotres-Alvarez D, *et al.* Maternal dietary patterns during pregnancy are associated with child growth in the first 3 years of life. *J Nutr* 2016; 146: 2281–2288.
22. Houde AA, St-Pierre J, Hivert MF, *et al.* Placental lipoprotein lipase DNA methylation levels are associated with gestational diabetes mellitus and maternal and cord blood lipid profiles. *J Dev Orig Health Dis* 2014; 5: 132–141.
23. Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. *Pediatrics* 2009; 124: S23–S34.

How to cite this article: Martin CL, Vladutiu CJ, Zikry TM, Grace MR, Siega-Riz AM. Maternal lipid levels during pregnancy and child weight status at 3 years of age. *Pediatric Obesity*. 2019;14:e12485. <https://doi.org/10.1111/ijpo.12485>