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Pro-inflammatory Diets During Pregnancy and Neonatal Adiposity in the Healthy Start Study

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Abstract

Objective: To evaluate the association between dietary inflammatory index (DII) scores during pregnancy and neonatal adiposity.

Study design: The analysis included 1,078 mother-neonate pairs in Healthy Start, a prospective pre-birth cohort. Diet was assessed using repeated 24-hour dietary recalls. DII scores were obtained by summing nutrient intakes, which were standardized to global means and multiplied by inflammatory effect scores. Air displacement plethysmography measured fat mass and fat-free within 72 hours of birth. Linear and logistic models evaluated the associations of DII scores with birth weight, fat mass, fat-free mass, and percent fat mass, and with categorical outcomes of small- and large-for-gestational age. We tested for interactions with pre-pregnancy BMI and gestational weight gain.

Results: The interaction between pre-pregnancy BMI and DII was statistically significant for birth weight, neonatal fat mass, and neonatal percent fat mass. Among neonates born to obese

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J.H. owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. N.S. Shivappa is an employee of CHI. The other authors declare no conflicts of interest.

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women, each one-unit increase in DII was associated with increased birth weight (53-g; 95% CI: 20, 87), fat mass (20-g; 95% CI: 7, 33), and percent fat mass (0.5%; 95% CI: 0.2, 0.8). No interaction was detected for small- and large-for-gestational age. Each one-unit increase in DII score was associated a 40% increase in odds of a large-for-gestational age neonate (1.4; 95% CI: 1.0, 2.0; p=0.04), but not a small-for-gestational age neonate (1.0; 95% CI: 0.8, 1.2; $P = .80$). There was no evidence of an interaction with gestational weight gain.

Conclusions: Our findings support the hypothesis that an increased inflammatory milieu during pregnancy may be a risk factor for neonatal adiposity.

Trial registration—Clinicaltrials.gov NCT02273297

Keywords

adiposity; fetal programming; pregnancy; dietary inflammatory index; inflammation

Future risk for obesity may manifest as early as 2 months of age,[1] which suggests that intrauterine exposures may predispose offspring to obesity.[2] An inflammatory milieu during pregnancy can result in fetal overgrowth.[3–6] In both human and animal pregnancies, exposure to inflammatory cytokines is associated with increased adiposity in offspring.[5, 6]

Pre-pregnancy obesity is an important contributing factor to neonatal adiposity and maternal sub-clinical inflammation may be a key mechanism.[7–10] Obesity is characterized by chronic, low-grade inflammation that is further exacerbated by metabolic changes during pregnancy.[11, 12] Fetuses from obese women are exposed to a pro-inflammatory environment during development,[4, 12–15] which may be associated with increased adiposity at birth.[16] Excessive gestational weight gain may also contribute to inflammation via maternal fat accumulation.[17]

A pro-inflammatory diet during pregnancy may alter risk for neonatal adiposity, especially in the context of pre-existent maternal obesity or excessive gestational weight gain. The dietary inflammatory index (DII) is an indicator of the overall inflammatory potential of an individual's diet.[18] The DII ranges from −9 (most anti-inflammatory) to +8 (most pro-inflammatory),[18] where higher DII scores are associated with increased circulation of inflammatory markers.[19–21] Higher DII scores may indicate a diet high in the consumption of processed meat and sugar-sweetened beverages, whereas lower DII scores may indicate a diet with ample servings of fruit, vegetables, whole grains, fish, and eggs.[20] Sen et al demonstrated that higher DII scores among women who were obese entering pregnancy is associated with an increase in odds of a small-for-gestational age neonate.[20] However, the impact of DII scores on neonatal adiposity is unknown.

Our goal was to evaluate the association between DII scores during pregnancy and neonatal adiposity, incorporating a direct measure of body composition. We hypothesized that a higher DII score would be associated with greater adiposity at birth, particularly among neonates born to obese mothers or mothers with excessive gestational weight gain.

Methods

The Healthy Start study recruited 1,410 pregnant women aged ≥16 years with singleton pregnancies enrolled before 24 weeks of gestation from the obstetrics clinics at the University of Colorado Hospital from 2009 through 2014. Participants completed research visits in early pregnancy (median 17 weeks gestation), mid-pregnancy (median 27 weeks gestation), and at delivery (median 1 day post-delivery). Additional inclusion criteria for this study included completion of at least one dietary recall, neonates born ≥32 weeks of gestation, those with complete body composition measures at birth, and those born to women with a pre-pregnancy body mass index (BMI)≥18.5 kg/m^2. The Healthy Start study protocol was approved by the Colorado Multiple Institutional Review Board. All women provided written informed consent before the first study visit. The Healthy Start study was registered as an observational study at clinicaltrials.gov as NCT02273297.

Fat mass and fat-free mass were measured using air displacement plethysmography (PEA POD, COSMED, Rome Italy) within ~72 hours of delivery. The PEA POD device measures body mass and volume, calculates body density, and estimates fat mass (g), fat-free mass (g), and percent fat mass. Each neonate was measured twice by trained research personnel, with a third measurement taken when percent fat mass differed by >2.0%. The average of the two closest readings was used for analysis.

We calculated sex-specific percentiles of birth weight for gestational age by using United States national reference data.[22] Neonatal size was defined as follows: small-for-gestational age (birth weight<10th percentile for age and sex), appropriate-for-gestational age (birth weight ≥10th percentile and ≤90th percentile for age and sex), and large-for-gestational age (birth weight >90th percentile for age and sex). For this analysis, appropriate-for-gestational age served as the reference category.

Maternal diet was measured throughout pregnancy using the Automated Self-Administered 24-hour Dietary Recall (ASA24), an online platform developed and hosted by the National Cancer Institute (ASA24-Beta and ASA24–2011, Bethesda, MD, USA). Healthy Start participants were asked to complete one dietary recall per month, beginning at the first study visit. Approximately 76% of the participants completed at least two dietary recalls over the pregnancy period (range: 1–8, median: 3). Trained, bilingual study staff members administered recalls in-person for Spanish-speaking participants (n=60) at study visits and over the phone between research visits. Data from the ASA24 were collected and processed by the Diet, Physical Activity and Body Composition Core of the Nutrition Obesity Research Center at the University of North Carolina at Chapel Hill. Individual nutrients were derived from the recalls using the USDA Food and Nutrient Database for Dietary Studies, versions 1.0 and 4.1.

The DII scores were based on 28 nutrients obtained from the 24-hour dietary recalls:[18] energy, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, omega-3 polyunsaturated fatty acids, omega-6 fatty acids, trans-fat, carbohydrates, fiber, protein, cholesterol, iron, Vitamin A, Vitamin C, Vitamin D, Vitamin E, niacin, thiamin, riboflavin, Vitamin B6, Vitamin B12, folic acid, magnesium, zinc, selenium, alcohol, and caffeine.

Inflammatory effect scores were computed for each of the 28 nutrients based on ~6,500 peer-reviewed articles (Figure 1; available at www.jpeds.com). Inflammatory effect scores were derived by first assigning "+1" to anti-inflammatory nutrients and "−1" to pro-inflammatory nutrients and then adjusting the scores by the total number of articles that cited its pro- or anti-inflammatory effects. The inflammatory effect scores indicate the relative contribution of each nutrient to the final DII score, where fiber is the most anti-inflammatory nutrient and saturated fat is the most pro-inflammatory nutrient.

The DII score for each dietary recall was obtained by standardizing the nutrient intakes to global means, multiplying by the appropriate inflammatory effect scores, and taking the sum of the 28 nutrients.[18] For women with more than one dietary recall, the DII scores were averaged across the entire pregnancy.

Maternal height was measured using a stadiometer at the first research visit by research personnel. Pre-pregnancy weight was obtained from medical records (91%) or from questionnaires completed at the early pregnancy research visit (9%). Previous studies have reported strong agreement between self-reported pre-pregnancy weight and pre-pregnancy weights obtained from medical records or study data.[23, 24] Pre-pregnancy BMI was calculated as pre-pregnancy weight (kg) divided by height (m) squared. Pre-pregnancy BMI categories were defined as follows: lean (BMI>18.5 kg/m2 and <25 kg/m2), overweight (BMI>25 kg/m^2 and <30 kg/m^2), and obese (BMI≥30 kg/m^2).[25]

Gestational weight gain was calculated as the difference between the last available weight measurement during pregnancy (measured by research staff or medical personnel) and the pre-pregnancy weight (described above). Gestational weight gain was categorized as less than recommended, within the recommended range, and greater than based on the 2009 Institute of Medicine guidelines.[26]

In a subset of the Healthy Start cohort, inflammatory markers interleukin-6 (IL-6) and high-sensitivity C-reactive protein (CRP-hs) were measured in maternal blood samples, collected at a median gestational age of 27 weeks. IL-6 was measured using Luminex MAP technology (R&D Systems, Inc.). CRP-hs was measured using immunoturbidimetric methodology (Beckman Coulter, Inc). Laboratory analyses were conducted at the University of Colorado Hospital Clinical and Translational Research Center Core Laboratory.

Data on maternal education, household income, and race/ethnicity were collected through research questionnaires. Maternal age at delivery was calculated from delivery date and maternal date of birth. Gestational age at delivery was abstracted from medical records or calculated based on the offspring delivery date and the offspring due date. Physical activity in pregnancy was measured using the Pregnancy Physical Activity Questionnaire.[27] Metabolic equivalent task (MET) values were estimated as described in detail elsewhere.[28]

Statistical analyses:

One-way analysis by variance (ANOVA) tests were used to examine differences in means and chi-square tests were used to examine differences in proportions across the pre-pregnancy BMI categories. Linear regression models estimated the associations of DII

scores during pregnancy with IL-6 or CRP-hs in a sub-sample. Linear regression models examined the association between DII scores during pregnancy on birth weight (g), neonatal fat mass (g), neonatal fat-free mass (g), and neonatal adiposity (percent fat mass) as separate outcomes. A multinomial logistic regression model was used to simultaneously examine the association between DII scores during pregnancy on small- and large-for-gestational age neonates (with appropriate-for-gestational age neonates as the reference category). Interaction was assessed by introducing product terms between pre-pregnancy BMI or gestational weight gain with DII scores into separate models.

Covariates were identified a priori based on the literature.[9, 20] Our final models adjusted for maternal race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), maternal education (<high school, high school diploma, some college), household income (<$40,000, $40,001 to $70,000, >$70,000, missing/do not know), smoking during pregnancy (yes, no), offspring sex, gestational age (weeks), gestational weight gain (kg), total caloric intake (kcal/day), and average energy expenditure (METs/week). Adjusted beta coefficients or odds ratios with corresponding 95% confidence intervals (CIs) were presented for our final models. An alpha level of 0.05 was used to determine statistical significance. All analyses were performed using Stata, version 14 (StataCorp LP).

Results

Of the 1,410 women eligible for the current analysis, 1,366 women completed at least one dietary recall during pregnancy. Of the remaining women, we excluded 42 mothers with a pre-pregnancy BMI<18.5 kg/m^2 and 24 women due to neonates born at <32 weeks of gestation. Of these women, 1,078 of the offspring had complete body composition measures at birth (Figure 2; available at www.jpeds.com). Included mother-neonate dyads (n=1,078) and excluded mother-neonate dyads (n=332) were similar with respect to maternal age at delivery, maternal race/ethnicity, pre-pregnancy BMI categories, and household income (results not presented). Of these women, 511 had IL-6 and CRP-hs measured in blood samples taken at 27 weeks gestation.

Maternal and neonatal characteristics are presented in Table I. A majority of the women included in our study were classified as lean entering pregnancy (n=580, 54%). A total of 281 women (26%) were classified as overweight and 217 women (20%) were classified as obese entering pregnancy. Women who were lean entering pregnancy were more likely to gain weight within the recommended range (p<0.01). Women who were obese entering pregnancy were more likely to be Hispanic or non-Hispanic Black (p<0.01), to have an annual household income below $40,000 (p<0.01), and to have attended college (p<0.01). Lean, overweight, and obese women were similar with respect to maternal age (p=0.78) and self-report of any smoking during pregnancy (p=0.12).

The mean DII score was +0.4 with a range from −4.4 to +4.0. Women who were classified as overweight entering pregnancy consumed fewer calories than women who were lean or obese entering pregnancy (p<0.01). Women who were classified as lean entering pregnancy consumed more carbohydrates (p<0.01) and more total fat (p=0.03) than women who were overweight or obese entering pregnancy. We did not find evidence of a difference in the

consumption of protein across the pre-pregnancy BMI categories (p=0.14). The gestational age at delivery was slightly greater among lean women as compared with overweight or obese women (p=0.02).

Individual nutrients had moderate to high correlations with DII scores (Table 2;available at www.jpeds.com). Fiber, vitamin E, and magnesium contributed the most to the DII score (Spearman rank correlation coefficients of −0.87, −0.80, and −0.87, respectively). Conversely, intake of caffeine and alcohol contributed the least to the total DII score (Spearman rank correlation coefficients of −0.17 and −0.14, respectively). Total energy, protein, total fat, saturated fat, and carbohydrates were moderately associated with the DII score (Spearman rank correlation coefficients ranging from of −0.40 to −0.64). Pre-pregnancy BMI and gestational weight gain were weakly associated with the DII score (Spearman rank correlation coefficients of 0.18 and −0.04, respectively). The correlation coefficients among women with at least two dietary recalls (n=879) were similar to the correlation coefficients among all women included in our analyses (n=1,078).

The mean IL-6 was 1.79±1.61mg/L with a range of 0.39 mg/L through 23.74 mg/L. Each 1-unit increase in DII score was associated with a 0.12-mg/L increase in IL-6 levels (95% CI: 0.01, 0.24; p=0.03), after adjustment for pre-pregnancy BMI, education, household income, maternal age, parity, race/ethnicity, and smoking during pregnancy. We did not detect an interaction between DII scores and pre-pregnancy BMI on IL-6 levels (p for interaction=0.77). DII scores were not associated with CRP-hs (b=0.29, 95% CI: −0.22, 0.80; p=0.27).

Although patterns were generally in the expected direction, there was limited evidence that the DII score was independently related to birth weight, neonatal fat mass, neonatal fat-free mass, or neonatal percent fat mass in the entire study population (Table 3). The interaction between pre-pregnancy BMI and DII score was statistically significant for the outcomes of birth weight, fat mass, and percent fat mass. Among neonates born to obese women, each one-unit increase in DII score was associated with increased birth weight (59-g; 95% CI: 11, 111), neonatal fat mass (24-g; 95% CI: 3, 44), and neonatal percent fat mass (0.5%; 95% CI: 0.0, 1.0), but not neonatal fat-free mass (37-g; 95% CI: −1, 75). Among women who were obese entering pregnancy, consuming a highly pro-inflammatory diet (DII score of +4.0) may result in a 472-g increase neonatal birth weight and 192-g increase in neonatal fat mass as compared with consuming a highly anti-inflammatory diet (DII score of −4.0). No such associations were observed among neonates born to women who were lean or overweight entering pregnancy. No interaction between gestational weight gain and the DII score was detected for the outcomes of birth weight, neonatal fat mass, neonatal fat-free mass, and neonatal percent fat mass.

There was a main effect association between the DII score for the outcome of large-forgestational age (Table 4). Each one-unit increase in DII score was associated with a 40% increase in odds of a large-for-gestational age neonate (95% CI: 1.0, 1.9; p=0.05). The results do not support the hypothesis that an increased DII score is associated with a small-for-gestational age neonate (0.9; 95% CI: 0.8, 1.1; p=0.50). There was no evidence of an

interaction between DII scores with pre-pregnancy BMI or gestational weight for the outcomes of small- or large-forgestational age.

Discussion

We observed that among women who were obese entering pregnancy, a pro-inflammatory diet during pregnancy was associated with increased neonatal adiposity. However, no such association was observed among neonates of lean or overweight women. Our findings support the hypothesis that a pro-inflammatory diet during pregnancy in the context of pre-existent maternal obesity may be a risk factor for alter risk for neonatal adiposity.

The extent to which the DII score reflects diet-induced inflammation in pregnancy has been relatively understudied. In adult men and non-pregnant women, higher DII scores are associated with increased circulation of CRP[19] and IL-6.[21] Only one published study has examined the association between DII scores and inflammatory markers during pregnancy. In Project Viva, Sen et al demonstrated that higher DII scores were associated with increased circulation of CRP.[20] We observed that higher DII scores were associated with increased circulation of IL-6, but not hs-CRP, at 27 weeks of gestation. The production of CRP may depend on IL-6 secretion;[29] therefore, we speculate that the associations may depend on the timing of the cytokine measurement.

In our cohort, we demonstrate that a higher DII score during pregnancy is associated with an increase in odds of a large-for-gestational age neonate. By contrast, in the Project Viva cohort, Sen et al observed that among women who were obese entering pregnancy a higher DII score during pregnancy is associated with an increase in odds of a small-for-gestational age neonate.[20] There are several factors that could explain the discrepancy. Sen et al examined this association among a well-educated population with a mean DII score of −2.6±1.4, indicating that many pregnant women in Project Viva consumed a relatively anti-inflammatory diet during pregnancy.[20] We reported a mean DII score of +0.4±1.5, which indicates that many of the pregnant women in Healthy Start consumed a more pro-inflammatory diet during pregnancy. Our results may be more generalizable to the overall pregnant population in the United States, because the mean DII score observed in our study is comparable with the mean DII score previously reported among men and women who participated in the 2005–2010 National Health and Nutrition Examination Survey (+0.9±1.1).[30] The discrepancy may also be due to differences in the methods of dietary assessment. In Project Viva, diet was assessed using a first-trimester and second-trimester food frequency questionnaire,[20] whereas in Healthy Start, diet was measured throughout pregnancy by 24-hour recalls. Further investigation in other large, diverse birth cohorts is warranted to assess the impact of a higher DII score during pregnancy on neonatal size and adiposity.

Maternal inflammation during pregnancy is associated with increased offspring size at birth,[3–6] but mechanisms remain uncertain. Both diet-induced and obesity-induced inflammation during pregnancy may play a role. Diet-induced inflammation during pregnancy may contribute to fetal fat accretion via fetal lipotoxicity[31] and/or functional changes to fetal adipose tissue of the offspring.[32, 33] Similarly, the chronic inflammatory environment

induced by maternal obesity may influence fetal fat accretion by increasing glucose and lipid availability[34] or increasing the number of adipocytes among the offspring.[16, 35] The potential mechanisms responsible for the complex inter-relationships between maternal diet, obesity, inflammation, and offspring adiposity need to be further explored in mechanistic studies.

One limitation of our approach is the use of self-reported dietary intake data. The pregnant women in our study may have failed to accurately report food frequency or quantity.[36] However, a distinct advantage of Healthy Start is the use of repeated 24-hour recalls of diet to estimate the average DII score during pregnancy (range: 1–8; median: 3), which has been shown to improve the validity of dietary recalls.[37]

Another limitation is the inability to establish whether inflammation specifically mediated the association between a pro-inflammatory diet during pregnancy and neonatal adiposity, given the smaller sample with available inflammatory biomarkers in our study. A pro-inflammatory diet during pregnancy may act through several biological, metabolic, or genetic mechanisms to increase neonatal adiposity.[38] Although a number of mechanisms may play a role, inflammation appears to be an important mechanism of these associations. Our results indicate that the DII was associated with greater IL-6, which supports the hypothesized effect of maternal diet on neonatal adiposity via systemic inflammation. Furthermore, our identification of statistical interaction with pre-pregnancy obesity supports the hypothesis that an increased inflammatory milieu during pregnancy may be a risk factor for neonatal adiposity.

One strength of our study is the ability to examine the association between DII scores during pregnancy and neonatal adiposity, incorporating a high quality measure of neonatal body composition. Healthy Start used air displacement plethysmography, which has been shown to provide more accurate estimates of neonatal adiposity than birth weight or other indirect measures of body composition.[39–41]

In conclusion, we provide evidence for an association between a pro-inflammatory diet during pregnancy and fetal fat accretion among women who were obese entering pregnancy. These findings suggest that consuming an anti-inflammatory diet during pregnancy may ameliorate maternal obesity-induced programming of adiposity in the next generation, a hypothesis that requires future testing.

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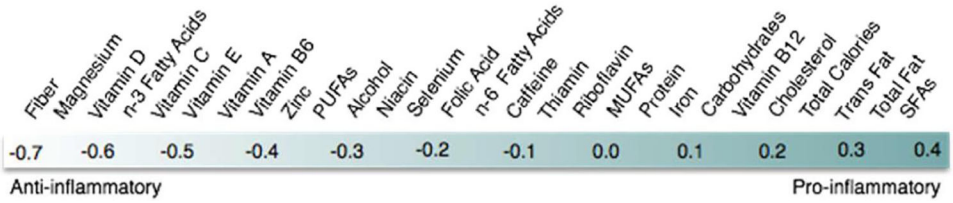

Figure 1;

Online Only. Inflammatory effect scores of nutrients included in the DII

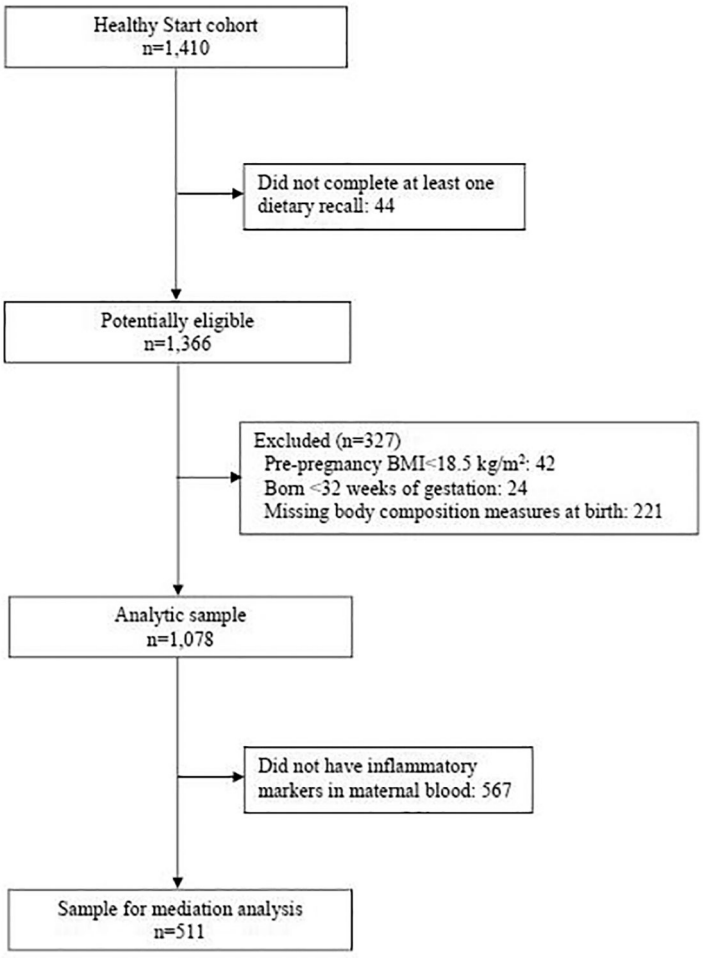

Figure 2;
Online Only. Study population and exclusion

Table 1.

Characteristics of participants in the Healthy Start study, Colorado, 2010–2014.

		Pre-pregnancy BMI category			
	Total (n=1,078)	**Lean (n=580)**	**Overweight (n=281)**	**Obese (n=217)**	**p-value**
Maternal characteristics					
Maternal age, yrs	28±6	29±6	28±6	28±6	0.78
Pre-pregnancy BMI, kg/m^2	29±6	22±2	27±1	36±6	<0.01
Gestational weight gain categories					
Less than recommended	21%	24%	12%	23%	
Within recommended range	29%	35%	23%	24%	
More than recommended	50%	41%	65%	55%	<0.01
Maternal Race/Ethnicity					
Non-Hispanic white	54%	65%	49%	38%	
Non-Hispanic black	15%	12%	13%	20%	
Hispanic	25%	17%	35%	36%	
Other	6%	7%	4%	5%	<0.01
Household income					
<$40,000	29%	22%	30%	47%	
$70,001 to $70,000	18%	18%	29%	16%	
>$70,000	34%	42%	30%	17%	
Don’t know	18%	18%	22%	17%	<0.01
Mother’s highest level of education					
<12 years	14%	12%	14%	16%	
High school degree	17%	14%	15%	29%	
College classes or college degree	70%	74%	70%	55%	<0.01
Maternal smoking during pregnancy					
No	92%	92%	94%	89%	
Yes	8%	8%	6%	11%	0.12
Average energy expenditure, METs/week	186±87	193±95	179±79	177±77	p<0.01
Maternal diet during pregnancy					
DII score	0.4±1.5	0.2±1.6	0.7±1.5	0.9±1.5	<0.01

	Pre-pregnancy BMI category				
	Total (n=1,078)	**Lean (n=580)**	**Overweight (n=281)**	**Obese (n=217)**	**p-value**
Total energy, kcal/day	2,035±701	2,105±700	1,692±694	1,944±702	<0.01
Protein, g/day	82±29	83±28	80±30	80±31	0.14
Carbohydrate, g/day	256±93	267±92	243±94	242±91	<0.01
Total fat, g/day	80±34	82±34	78±33	77±34	0.03
Neonate characteristics					
Male offspring	52%	50%	53%	56%	0.29
Gestational age at birth, wks	40±1	40±1	39±1	39±1	0.02

Abbreviations: BMI, body mass index; DII, dietary inflammatory index; MET, metabolic equivalent task.

Continuous variables are expressed as the mean±standard deviation. One-way analysis by variance (ANOVA) tests were used to examine differences in means across the pre-pregnancy BMI categories. Categorical variables are express as proportions of column totals. Chi-square tests were used to examine differences in proportions across the pre-pregnancy BMI categories.

[a]Pre-pregnancy BMI categories were defined as follows: lean (BMI≥18.5 and <25 kg/m^2), overweight (BMI≥25) and <30 kg/m^2), and obese (BMI≥30 kg/m^2).

Table 2;

Online Only. Correlation between daily intake of individual nutrients and DII score in the Healthy Start study, Colorado, 2010–2014.

	Correlation with DII Score		Mean±SD of individual nutrients		
	All women (n=1,078	Women with >1 dietary recall (n=879)	All women (n=1,078)	Women with a more anti-inflammatory diet (DII<median value) (n=542)	Women with a more pro-inflammatory diet (DII>median value) (n=536)
DII Score	-	-	0.4±1.5	−0.8±0.9	1.7±0.8
Pre-pregnancy BMI (kg/m^2)	0.18	0.17	26±6	25±6	27±6
Gestational weight gain (kg)	−0.04	0.02	14±7	14±6	14±7
Total energy (kcal/d)	−0.64	−0.60	2035±701	2372±714	1702±502
Protein (g/day)	−0.59	−0.54	82±29	96±28	69±24
Carbohydrate (g/day)	−0.63	−0.57	256±93	300±95	212±67
Total fat (g/day)	−0.50	−0.47	80±34	93±36	67±25
Saturated fat (g/day)	−0.40	−0.32	30±13	32±13	24±11
Monounsaturated fat (g/day)	−0.52	−0.46	29±13	14±9	24±10
n-3 fatty acids (g/day)	−0.26	−0.88	0.03±0.08	0.04±0.07	0.03±0.08
Fiber (g/day)	−0.87	−0.65	18±8	24±7	13±4
Vitamin A (IU/day)	−0.62	−0.58	2370±2721	3520±3230	1231±1342
Vitamin C (mg/day)	−0.63	−0.59	109±94	141±108	77±65
Vitamin D (IU/day)	−0.31	−0.31	4.9±3.4	5.6±3.6	4.1±2.9
Vitamin E (mg/day)	−0.80	−0.81	7.6±4.0	9.9±4.1	5.2±2.1
Niacin (mg/day)	−0.59	−0.55	23±9	27±9	19±7
Thaimin (mg/day)	−0.61	−0.56	1.7±0.7	2.0±0.7	1.4±0.5
Riboflavin (mg/day)	−0.61	−0.52	2.2±0.9	2.6±0.8	1.8±0.7
Vitamin B6 (mg/day)	−0.72	−0.67	2.0±0.9	2.5±0.8	1.5±0.6
Vitamin B12 (mg/day)	−0.37	−0.31	5.3±2.8	6.2±2.9	4.5±2.5
Folic Acid (ug/day)	−0.30	−0.18	231±164	272±186	190±127
Magnesium (mg/day)	−0.87	−0.87	300±110	375±91	224±67
Selenium (ug/day)	−0.52	−0.46	108±40	125±37	92±36
Zinc (mg/day)	−0.59	−0.53	13±5	15±5	10±4
Iron (mg/day)	−0.60	−0.55	17±7	20±7	13±5
Alcohol (g/day)	−0.17	−0.15	0.1±1.2	0.1±0.6	0.2±1.6

	Correlation with DII Score		Mean±SD of individual nutrients		
	All women (n=1,078	Women with >1 dietary recall (n=879)	All women (n=1,078)	Women with a more anti-inflammatory diet (DII<median value) (n=542)	Women with a more pro-inflammatory diet (DII>median value) (n=536)
Caffeine (mg/day)	−0.14	−0.09	36±49	40±52	31±45

Abbreviations: BMI, body mass index; DII, dietary inflammatory index; SD, standard deviation.

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Table 3.

Associations between DII scores with neonatal adiposity among 1,078 mother-neonate pairs in the Healthy Start study, Colorado, 2010–2014.

	Adjusted[a] beta coefficients for each one-unit increase in DII score (95% CI)			
	Birth weight (g)	**Fat mass (g)**	**Fat-free mass (g)**	**Percent fat mass**
Model 1: All	9 (12, 30); p=0.40	5 (−3, 14); p=0.19	4 (−12, 20); p=0.64	0.1 (−0.1, 0.4); p=0.17
Model 2: Interaction with pre-pregnancy BMI				
Lean (n=580)	−3 (−30, 24); p=0.82	0 (−10, 11); p=0.97	−3 (−23, 18); p=0.78	0.0 (−0.2, 0.3); p=0.75
Overweight (n=281)	8 (−36, 51); p=0.72	7 (−11, 24); p=0.43	−2 (−37, 33); p=0.91	0.2 (−0.2, 0.7); p=0.27
Obese (n=217)	59 (7, 111); p=0.03	24 (3, 44); p=0.03	37 (−1, 75); p=0.06	0.5 (0.0, 1.0); p=0.04
p for interaction[b]	p=0.04	p=0.02	p=0.26	p=0.03
Model 3: Interaction with gestational weight gain				
Less than recommended (n=228)	−4 (−50, 42); p=0.85	2 (−13, 17); p=0.77	−13 (−50, 23); p=0.48	0.1 (−0.3, 0.5); p=0.60
Within recommended range (n=316)	−6 (−46, 34); p=0.75	9 (−7, 25); p=0.26	−16 (−46, 13); p=0.28	0.4 (−0.1, 0.8); p=0.10
More than recommended (n=534)	26 (−4, 56); p=0.09	7 (−6, 19); p=0.30	24 (1, 46); p=0.04	0.1 (−0.2, 0.4); p=0.49
p for interaction[c]	p=0.54	p=0.08	p=0.87	p=0.10

Abbreviations: BMI, body mass index; CI, confidence interval; DII, dietary inflammatory index.

[a]Adjusted for maternal age (years), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), household income (<$40,000, $40,001 to $70,000, >$70,000, missing/do not know), smoking during pregnancy (yes, no), offspring sex, gestational age (weeks), total energy (kcal/day), and average energy expenditure (metabolic equivalent task [MET]/week). Models 1 and 2 additionally adjusted for gestational weight gain (kg). Models 1 and 3 additionally adjusted for pre-pregnancy BMI (kg/m^2).

[b]The p-value for interaction was determined by including an interaction term between pre-pregnancy BMI and DII score in linear regression models with total mass, fat mass, fat-free mass, and adiposity as separate outcomes.

[c]The p-value for interaction was determined by including an interaction term between gestational weight gain and DII score in linear regression models with total mass, fat mass, fat-free mass, and adiposity as separate outcomes.

Table 4.

Associations between DII scores with weight for gestational age[a] among 1,078 mother-neonate pairs in the Healthy Start study, Colorado, 2010–2014.

	Adjusted[b] odds ratio for each one-unit increase in DII score (95% CI)	
	Small for gestational age vs. appropriate for gestational age	**Large for gestational age vs. appropriate for gestational age**
Model 1: All	0.9 (0.8, 1.1); p=0.50	1.4 (1.0, 1.9); p=0.05
Model 2: Interaction with pre-pregnancy BMI		
Lean (n=580)	1.1 (0.9, 1.3); p=0.38	1.7 (0.6, 2.1); p=0.61
Overweight (n=281)	0.9 (0.7, 1.2); p=0.56	1.2 (0.6, 2.3); p=0.60
Obese (n=217)	0.9 (0.6, 1.3); p=0.56	1.6 (0.7, 3.2); p=0.24
p for interaction[c]	p=0.28	p=0.36
Model 3: Interaction with gestational weight gain		
Less than recommended (n=228)	1.0 (0.7, 1.4); p=0.97	0.7 (0.1, 8.0); p=0.79
Within recommended range (n=316)	1.2 (0.8, 1.7); p=0.33	1.7 (0.7, 4.3); p=0.26
More than recommended (n=534)	0.9 (0.7, 1.1); p=0.29	1.3 (0.8, 1.9); p=0.27
p for interaction[d]	p=0.93	p=0.29

Abbreviations: BMI, body mass index; CI, confidence interval; DII, dietary inflammatory index.

[a]We calculated sex-specific percentiles of birth weight for gestational age by using United States national reference data. Neonatal size was defined as follows: small for gestational age (birth weight<10th percentile for age and sex), appropriate for gestational age (birth weight≥10th percentile and ≤90th percentile for age and sex), and large for gestational age (birth weight >90th percentile for age and sex).

[b]Adjusted for maternal age (years), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), household income (<$40,000, $40,001 to $70,000, >$70,000, missing/do not know), smoking during pregnancy (yes, no), offspring sex, gestational age (weeks), total energy (kcal/day), and average energy expenditure (metabolic equivalent task [MET]/week). Models 1 and 2 additionally adjusted for gestational weight gain (kg). Models 1 and 3 additionally adjusted for pre-pregnancy BMI (kg/m^2).

[c]The p-value for interaction was determined by including an interaction term between pre-pregnancy BMI and DII score in the multinomial logistic regression model.

[d]The p-value for interaction was determined by including an interaction term between gestational weight gain and DII score in the multinomial logistic regression model.