

# Pre-pregnancy obesity and maternal nutritional biomarker status during pregnancy: a factor analysis

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## Abstract

**Objective:** Pre-pregnancy obesity has been associated with adverse birth outcomes. Poor essential fatty acid (EFA) and micronutrient status during pregnancy may contribute to these associations. We assessed the associations between pre-pregnancy BMI and nutritional patterns of maternal micronutrient and EFA status during mid-pregnancy.

**Design:** A cross-sectional analysis from a prospective cohort study. Women provided non-fasting blood samples at  $\leq 20$  weeks' gestation that were assayed for red cell EFA; plasma folate, homocysteine and ascorbic acid; and serum retinol, 25-hydroxyvitamin D,  $\alpha$ -tocopherol, soluble transferrin receptors and carotenoids. These nutritional biomarkers were employed in a factor analysis and three patterns were derived: EFA, Micronutrients and Carotenoids.

**Setting:** The Antidepressant Use During Pregnancy Study, Pittsburgh, PA, USA.

**Subjects:** Pregnant women ( $n$  129).

**Results:** After adjustment for parity, race/ethnicity and age, obese pregnant women were 3.0 (95% CI 1.1, 7.7) times more likely to be in the lowest tertile of the EFA pattern and 4.5 (95% CI 1.7, 12.3) times more likely to be in the lowest tertile of the Carotenoid pattern compared with their lean counterparts. We found no association between pre-pregnancy obesity and the Micronutrient pattern after confounder adjustment.

**Conclusions:** Our results suggest that obese pregnant women have diminished EFA and carotenoid concentrations.

**Keywords**  
Nutrition  
Pregnancy  
Obesity  
Factor analysis

In the USA, nearly a quarter of all pregnancies are complicated by pre-pregnancy obesity and the prevalence is increasing<sup>(1)</sup>. Pregnant women who are obese are at higher risk of pre-eclampsia<sup>(2,3)</sup>, gestational diabetes mellitus<sup>(4)</sup>, birth trauma, large-for-gestational-age birth<sup>(2)</sup> and stillbirth<sup>(2,5)</sup> compared with their lean counterparts. Nevertheless, the mechanism by which obesity contributes to poor outcomes remains uncertain.

Nutritional status during pregnancy may partially mediate the relationship between pre-pregnancy obesity and adverse pregnancy and birth outcomes. In non-pregnant populations, obesity has been associated with insufficiencies of micronutrients, including vitamin E, vitamin C, vitamin D, folate, vitamin A and carotenoids<sup>(6,7)</sup>. Obese individuals may also have lower levels of essential fatty

acids (EFA)<sup>(8,9)</sup> than lean patients. But the relationship between obesity and nutritional biomarkers has not been thoroughly researched in pregnancy. Micronutrients and EFA play critical roles in the healthy physical and neurological development of the fetus and prevent conditions such as anaemia and neural tube defects<sup>(10,11)</sup>. Therefore, it is critical to explore these associations in pregnancy.

The objective of our study was to evaluate the association between pre-pregnancy BMI and patterns of nutritional biomarkers at  $\leq 20$  weeks' gestation.

## Methods and procedures

We conducted a secondary data analysis from the Antidepressant Use During Pregnancy (ADUP) Study, a

prospective cohort study of pregnancy in Pittsburgh, PA, USA. The details of this study have been described previously<sup>(12,13)</sup>. Pregnant women were recruited at  $\leq 20$  weeks' gestation. Eligible women had singleton gestations and women were excluded if they had psychosis, bipolar disorder, active substance use disorder, gestational exposure to benzodiazepines or prescription drugs in the category of D or X (other than selective serotonin reuptake inhibitors) defined by the US Food and Drug Administration, or pre-existing chronic diseases. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients were approved by the University of Pittsburgh Institutional Review Board. Written informed consent was obtained from all patients.

The ADUP Study recruited women from 2000 to 2007. In 2004, the study protocol was modified to include nutrition measures, including biomarker assessment in maternal blood. Of the 197 eligible women interviewed from 2004 to 2007, 130 (66%) provided a non-fasting blood sample at  $\leq 20$  weeks that was processed for a full panel of nutritional biomarkers. We excluded one woman with missing data for pre-pregnancy weight. Our final analytic sample was 129 women. Women included in the analysis were less likely to be nulliparous than women who were excluded for missing weight measurements or blood samples (33% *v.* 51%,  $P = 0.01$ ). Other maternal characteristics such as pre-pregnancy BMI, age, education, race, marital status, smoking status, employment status and diagnosed major depressive disorder did not differ significantly ( $P > 0.05$ ) between the two groups.

Our exposure of interest was general maternal adiposity before conception, measured using pre-pregnancy BMI (weight (kg)/height (m)<sup>2</sup>). Pre-pregnancy BMI was based on pre-pregnancy weight, self-reported at enrolment, and measured height. Because only four women in the sample were underweight (BMI  $< 18.5$  kg/m<sup>2</sup>), we categorized women into three groups: lean (BMI  $< 25.0$  kg/m<sup>2</sup>), overweight (BMI = 25.0–29.9 kg/m<sup>2</sup>) and obese (BMI  $\geq 30.0$  kg/m<sup>2</sup>)<sup>(14)</sup>. Our outcome of interest was maternal nutritional status, as measured by patterns of nutritional biomarkers. At enrolment, women provided a non-fasting blood sample. Blood samples were assayed for red cell EFA, plasma folate, plasma homocysteine, plasma ascorbic acid, serum retinol, serum 25-hydroxyvitamin D, serum  $\alpha$ -tocopherol, serum ferritin, serum soluble transferrin receptors and serum carotenoids using methods described previously<sup>(13,15)</sup>.

Women identified their race/ethnicity as non-Hispanic white, non-Hispanic African American and other. Because only four women self-identified as 'other', we combined the African American and the 'other' groups into a non-white category for analysis. Women were categorized as nulliparous or as having a previous live birth. A diagnosis of major depressive disorder was made using the Structured Clinical Interview for DSM-IV<sup>(16)</sup>. Educational status was

defined as having less than a high school education, some college, college degree and post-graduate education. Women were classified as unemployed or employed (which included women who worked full time, part time or occasionally). For marital status, 'married' included married or living as married and 'unmarried' included single, separated, widowed and divorced. Women were classified as current smokers if they smoked at all during pregnancy or non-smokers if they did not.

We used Pearson  $\chi^2$  tests and Student *t* tests to determine differences in maternal characteristics by pre-pregnancy BMI categories. To describe skewed biomarkers, we calculated geometric means and log-transformed biomarkers before statistical testing. We conducted a factor analysis on the fifteen untransformed maternal dietary biomarkers as described previously<sup>(13)</sup>. Three patterns were generated and assigned names based on the biomarkers that loaded heavily on the pattern. Each represents biologically meaningful correlations between biomarkers: pattern 1 'Essential Fatty Acids (EFA)', pattern 2 'Micronutrients' and pattern 3 'Carotenoids'. Pattern scores were categorized based on tertiles of the distribution.

Logistic regression was used to assess the independent associations between pre-pregnancy BMI and the likelihood of being in the lowest tertile of each nutritional pattern. Potential confounders were maternal age, race/ethnicity, parity, education, marital status, smoking status, employment and depression (diagnosed with the Structured Clinical Interview for DSM-IV<sup>(16)</sup>). Only parity, race/ethnicity and age met our *a priori* definition of confounding ( $\geq 10\%$  change in the odds ratio after excluding the covariate from the full model). Analyses were conducted using statistical software package Stata version 11.0.

## Results

The women in the cohort were primarily well-educated, non-Hispanic white, married, non-smokers and employed (Table 1). The mean pre-pregnancy BMI was 26.6 (SD 6.0) kg/m<sup>2</sup>. About half (49.6%) of the women were lean, 22.5% were overweight and 27.9% were obese. Obese women were less likely to have a college degree ( $P < 0.01$ ) and more likely to be nulliparous ( $P < 0.01$ ) and depressed ( $P = 0.03$ ) than lean women. Maternal age, race/ethnicity, marital status, smoking and employment did not differ significantly by pre-pregnancy BMI category.

In unadjusted analysis, women who were overweight before pregnancy had lower mean concentrations of plasma folate ( $P = 0.04$ ), plasma ascorbic acid ( $P = 0.01$ ), serum  $\beta$ -carotene ( $P = 0.01$ ) and serum  $\beta$ -cryptoxanthin ( $P = 0.02$ ) than lean women (Table 2). Compared with lean women, obese pregnant women had lower mean concentrations of red cell DHA ( $P < 0.01$ ), red cell arachidonic acid ( $P = 0.01$ ), plasma ascorbic acid ( $P = 0.03$ ),

**Table 1** Maternal characteristics of the study population, stratified by pre-pregnancy BMI; Antidepressant Use During Pregnancy Study, Pittsburgh, PA, USA

Characteristic	Total (n 129)		BMI < 25.0 kg/m <sup>2</sup> (n 64)		BMI = 25.0–29.9 kg/m <sup>2</sup> (n 29)		BMI ≥ 30.0 kg/m <sup>2</sup> (n 36)		P value*
	n	%	n	%	n	%	n	%	
Age (years)									0.14
Mean	30.3		30.6		31.6		28.7		
SD	5.6		5.8		4.4		5.9		
Race/ethnicity									
White	103	79.8	56	87.5	23	79.3	24	66.7	
African American	22	17.1	6	9.4	6	20.7	10	27.8	
Other	4	3.1	2	3.1	0	0.0	2	5.6	0.10
Parity									
0	43	33.3	33	51.6	23	79.3	30	83.3	
1–6	86	66.7	31	48.4	6	20.7	6	16.7	<0.01
Educational status									
≤High school	23	17.8	5	7.8	4	13.8	14	38.9	
Some college	25	19.4	12	18.8	4	13.8	9	25.0	
College degree	45	34.9	25	39.1	9	31.0	11	30.6	
Post-graduate education	36	27.9	22	34.4	12	41.4	2	5.6	<0.01
Marital status									
Married	95	73.6	48	75.0	25	86.2	22	61.1	
Unmarried	34	26.4	16	25.0	4	13.8	14	38.9	0.07
Smoking status									
Non-smoker	110	85.3	56	87.5	27	93.1	27	75.0	
Smoker	19	14.7	8	12.5	2	6.9	9	25.0	0.10
Employment status									
Employed	73	56.6	37	57.8	17	58.6	19	52.8	
Unemployed	56	43.4	27	42.2	12	41.4	17	47.2	0.86
Major depression†									
Not depressed	96	74.4	53	82.8	22	75.9	21	58.3	
Depressed	33	25.6	11	17.2	7	24.1	15	41.7	0.03

\*Based on Student's *t* test for maternal age and  $\chi^2$  test for the other covariates.

†As measured by the Structured Clinical Interview for DSM-IV<sup>(16)</sup>.

**Table 2** Mean\* maternal nutritional biomarkers at 20 weeks' gestation, stratified by pre-pregnancy BMI; Antidepressant Use During Pregnancy Study, Pittsburgh, PA, USA

Biomarker	BMI < 25.0 kg/m <sup>2</sup> (n 64)		BMI = 25.0–29.9 kg/m <sup>2</sup> (n 29)		P value†	BMI ≥ 30.0 kg/m <sup>2</sup> (n 36)		P value
	Mean	95% CI	Mean	95% CI		Mean	95% CI	
Red cell DHA (%)	3.4	2.7, 4.4	3.1	2.2, 4.2	0.58	1.9	1.3, 2.7	<0.01
Red cell AA (%)	13.0	11.4, 14.8	12.9	10.5, 15.8	0.95	9.3	7.3, 11.9	0.01
Red cell EPA (%)	0.33	0.28, 0.40	0.28	0.22, 0.35	0.30	0.25	0.18, 0.33	0.06
Plasma folate (ng/ml)	15.3	13.6, 17.2	12.5	10.7, 14.6	0.04	13.0	11.3, 15.1	0.08
Plasma ascorbic acid (μg/ml)	12.9	12.1, 13.7	10.4	8.7, 12.4	0.01	11.0	9.7, 12.4	0.03
Serum retinol (μg/ml)	0.50	0.48, 0.53	0.46	0.43, 0.50	0.11	0.47	0.43, 0.51	0.17
Serum 25(OH)D (nmol/l)	88.5	81.3, 96.3	77.8	63.1, 96.0	0.20	69.9	59.0, 82.9	0.01
Serum α-tocopherol (μg/ml)	0.07	0.06, 0.07	0.07	0.06, 0.08	0.72	0.07	0.06, 0.07	0.47
Serum β-carotene (μg/ml)	0.14	0.10, 0.19	0.06	0.04, 0.11	0.01	0.04	0.03, 0.06	<0.01
Serum homocysteine (μmol/l)	2.3	2.1, 2.6	2.3	2.1, 2.6	0.94	2.3	1.9, 2.7	0.75
Serum sTfR (nmol/l)	14.5	13.7, 15.4	15.9	14.5, 17.4	0.09	16.3	14.9, 17.7	0.03
Serum lutein + zeaxanthin (μg/ml)	0.14	0.12, 0.17	0.12	0.10, 0.14	0.17	0.08	0.06, 0.10	<0.01
Serum β-cryptoxanthin (μg/ml)	0.10	0.08, 0.13	0.06	0.04, 0.09	0.02	0.05	0.04, 0.07	<0.01
Serum lycopene (μg/ml)	0.30	0.26, 0.35	0.32	0.27, 0.37	0.76	0.28	0.23, 0.34	0.41

AA, arachidonic acid; 25(OH)D, 25-hydroxyvitamin D; sTfR, soluble transferrin receptors.

\*Geometric means, all values are presented as mean and 95% confidence interval.

†Student's *t* test, biomarkers log-transformed before tests were performed, BMI < 25.0 kg/m<sup>2</sup> is the reference group.

serum 25-hydroxyvitamin D ( $P=0.01$ ), serum β-carotene ( $P<0.01$ ), serum lutein + zeaxanthin ( $P<0.01$ ) and serum β-cryptoxanthin ( $P<0.01$ ) and higher mean serum soluble transferrin receptors concentration ( $P=0.03$ ).

In unadjusted analysis, obese women had significantly greater odds of being in the lowest tertile of all three nutritional patterns. After adjustment for confounders,

obese pregnant women were three and five times more likely to be in the lowest tertile of the EFA and Carotenoid pattern, respectively, than lean women (Table 3). After adjustment, there was no association between obesity and Micronutrient pattern score. There was no relationship between pre-pregnancy overweight and any pattern before or after adjustment.

**Table 3** Association between pre-pregnancy BMI and the lowest tertile\* of each nutritional pattern; Antidepressant Use During Pregnancy Study, Pittsburgh, PA, USA

	Nutrient pattern (n 129)					
	Essential Fatty Acids		Micronutrient		Carotenoid	
	OR	95% CI	OR	95% CI	OR	95% CI
Unadjusted model						
BMI < 25.0 kg/m <sup>2</sup>		Ref.		Ref.		Ref.
BMI = 25.0–29.9 kg/m <sup>2</sup>	1.6	0.6, 4.1	2.5	1.0, 6.5	1.4	0.5, 3.7
BMI ≥ 30.0 kg/m <sup>2</sup>	2.7	1.1, 6.4	3.6	1.5, 8.6	5.0	2.1, 12.2
Adjusted model†						
BMI < 25.0 kg/m <sup>2</sup>		Ref.		Ref.		Ref.
BMI = 25.0–29.9 kg/m <sup>2</sup>	1.5	0.6, 4.1	1.8	0.6, 5.7	1.4	0.5, 4.3
BMI ≥ 30.0 kg/m <sup>2</sup>	3.0	1.1, 7.7	1.5	0.5, 4.5	4.5	1.7, 12.3

Ref, referent category.

\*Lowest tertile compared to the combined middle and highest tertiles of nutrient components.

†Adjusted for parity, race/ethnicity and age. Further adjustment for other covariates had no meaningful impact on the findings.

## Discussion

Using factor analysis of an array of nutritional biomarkers, we found that a larger percentage of obese women were in the lowest tertile of the EFA, Micronutrient and Carotenoid patterns than lean women at ≤20 weeks' gestation. After adjustment for maternal characteristics, pre-pregnancy obesity remained associated with poorer EFA and Carotenoid patterns.

To our knowledge, the present study is the first one to examine pre-pregnancy BMI relative to a wide range of maternal biomarkers. Our EFA and carotenoid conclusions are in agreement with previous studies of individual biomarkers in a variety of non-pregnant populations<sup>(7,17–20)</sup>. For example, in a cross-sectional analysis of 4512 non-pregnant women, both obese and overweight women were significantly more likely to be in the lowest 20th percentile of a sum of carotenoid concentrations than lean women<sup>(6)</sup>. Although we observed that obesity was associated with lower Micronutrient pattern scores in unadjusted analysis, adjustment for parity, race/ethnicity and age eliminated this effect. In contrast, other researchers have reported poorer micronutrient concentrations among obese women in non-pregnant populations<sup>(6,21)</sup>. One study of non-pregnant women found that obese women were more likely to have low levels of vitamin E, vitamin C, vitamin D and serum folate than non-obese women<sup>(6)</sup>. Studies in pregnancy report that maternal obesity increases the likelihood of poor maternal vitamin D<sup>(22)</sup> and folate<sup>(23)</sup> status in pregnancy. The differences in our conclusions may be due in part to prenatal vitamin use. While prenatal vitamins always contain micronutrients, they do not uniformly contain EFA or many carotenoids. Given the high socio-economic status of our population, the use of prenatal vitamins and other dietary supplements may have been widespread, leading to a predominance of elevated micronutrient concentrations. If obese women in our cohort were taking prenatal supplements but consumed diets poor in fish, the major

source of DHA and EPA, or fruits and vegetables, which contribute to carotenoids<sup>(24)</sup>, this may account for our results. Unfortunately, complete data on dietary intake and supplementation were not available at 20 weeks' gestation in the ADUP Study.

In addition to diet and supplementation differences between obese and lean pregnant women, pre-pregnancy obesity may alter the absorption and metabolism of carotenoids and EFA. It has been previously hypothesized that fat-soluble nutrients, such as carotenoids, may also be sequestered by adipose tissue<sup>(25)</sup>. However, among the individual nutritional biomarkers that had lower concentrations in obese women, we did not find a distinct pattern between the lipid-soluble and water-soluble markers.

Major strengths of our study include an analysis of a wide array of measured nutritional biomarkers. The use of factor analysis accounted for inherent correlations between nutrients and reduced the likelihood of type 1 error due to multiple comparisons. Our study was limited by self-reported weight to calculate BMI, which may have contributed to non-differential misclassification<sup>(26)</sup>. While we had a relatively small sample size of primarily white, well-educated, non-smoking women, we do not expect the biological associations between nutritional biomarkers and pre-pregnancy BMI to alter based on these factors. Our lack of longitudinal biomarker measurements limits our understanding of the temporality of these relationships. Large, prospective studies with repeated biomarker measures and detailed information on supplement use during pregnancy are needed to determine the extent of the association between maternal obesity and poor nutritional status.

Our results suggest that obese pregnant women have diminished EFA and carotenoid status during pregnancy. A better understanding of the effect of pre-pregnancy obesity on maternal micronutrient and EFA status may lead to specific nutritional interventions that can improve pregnancy and birth outcomes in this at-risk population.

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