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Allostatic load may not be associated with chronic stress in pregnant women, NHANES 1999–2006

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Abstract

Purpose—Pregnant women are generally excluded from studies that measure allostatic load (AL) because there is concern that the changing levels of AL-related biomarkers during pregnancy do not reflect a woman's true AL. The goal of this study was to determine whether AL can be measured in a meaningful way during pregnancy.

Methods—The National Health and Nutrition Examination Survey (NHANES) is a nationally representative, cross-sectional survey of the U.S. civilian population. AL was based on the distributions of 10 biomarkers in pregnant ($n = 1138$) and nonpregnant ($n = 4993$) women aged 15 to 44 from NHANES (1999–2006).

Results—The distribution of each AL-related biomarker differed significantly between pregnant and nonpregnant women ($P < .01$). Among nonpregnant women, high AL findings were consistent with previous studies (e.g., higher AL in women who are black, are older, and who have lower incomes). However, these associations were not seen in pregnant women.

Conclusions—Our results suggest that the various biomarkers that comprise AL may reflect proximal factors in pregnancy more strongly than they represent exposure to chronic stress over a woman's lifetime. Therefore, our approach to measuring AL may not provide meaningful information about chronic stress in pregnant women without further consideration of pregnancy-related factors.

Keywords

Allostasis; Stress; Psychological; Pregnancy complications

Introduction

Chronic psychosocial stress has been identified as a risk factor for adverse birth outcomes, including preterm birth, low birth-weight, and miscarriage [1,2]. However, the mechanism by which chronic stress impacts these outcomes remains unclear. The concept of allostatic load (AL) may help to explain adverse birth outcomes in women without other known risk factors [3].

AL is considered a measure of the cumulative “wear and tear” on the body resulting from exposure to chronic stress [4]. Chronic stress accelerates effects related to aging through a process known as “weathering,” and these effects accumulate differently in people of different races and socioeconomic circumstances [5,6]. Although AL has been associated with the risk of numerous health outcomes, only two studies have examined AL in relation to women’s reproductive health [7,8].

Pregnant women are generally excluded from studies that measure AL because there is concern that the changing levels of AL-related biomarkers during pregnancy do not reflect a woman’s true AL [9]. Pregnancy changes the levels of many factors related to AL, including cardiovascular, metabolic, and inflammatory markers [10]. However, these factors change in predictable ways, so measuring AL empirically during pregnancy may still reflect the effects of chronic stress over a woman’s lifetime. We hypothesized that, if AL scores in pregnancy represent a woman’s true AL, then AL will have similar characteristics in pregnant and nonpregnant women. To our knowledge, this study is the first to assess the usefulness of measuring AL during pregnancy in a nationally representative sample of women.

Methods

Sample

We used demographic and laboratory data from the National Health and Nutrition Examination Survey (NHANES), an ongoing study conducted by the National Center for Health Statistics. Participants in NHANES are selected from the general public and the survey sample is weighted to represent the civilian, noninstitutionalized U.S. population. Data are collected via an in-home interview and a clinical examination, and nationally representative results are made available for download in 2-year cycles [11]. Our sample consists of pregnant (n = 1138) and nonpregnant (n = 4993) women aged 15 to 44 who participated in NHANES between 1999 and 2006 [12].

AL-Related biomarkers

There is no single, “gold-standard” approach to operationalizing AL [13]. We selected 10 biomarkers based on their inclusion in previous AL studies [5,9,14,15] and their availability

in the NHANES data set. These biomarkers represent metabolic, immune, and cardiovascular factors (Table 1).

AL Index

The levels of each biomarker comprising the AL index change in predictable ways during pregnancy; for example, albumin and creatinine levels decline, and high-density lipoprotein cholesterol levels increase [10]. To account for these changes, we used empirical cutoff points to establish “low-” and “high-risk” values for each biomarker. In pregnant women, the cutoff points were based on the distribution of each biomarker in the sample of pregnant women. Similarly, the cutoff points in nonpregnant women were based on the distribution of each biomarker in the sample of nonpregnant women.

Our empirical approach to scoring AL was similar to that of previous AL studies [5,9,15–17]. Participants in the high-risk quartile for each biomarker were given a score of 1 for that biomarker; the others were given a score of 0. For most AL-related biomarkers, high-risk values represented the top 25% of the distribution. However, for albumin and high-density lipoprotein cholesterol, high-risk values were those in the bottom 25% of the distribution. Scores for each biomarker were summed to create an AL score ranging from 0 to 10 for each participant.

Sociodemographic factors

Sociodemographic factors included age, race, income, and education level. Age was categorized into 5-year intervals except for the oldest group, 35 to 44, which was expanded because fewer pregnant women are older than 35. Race was based on NHANES categories: Non-Hispanic white, non-Hispanic black, Mexican American, and other. Income was measured as a categorical variable based on ratio of family income to poverty. Education level followed NHANES categories: Less than high school, high school, and more than high school.

Sociodemographic factors were analyzed using a binary high/low measure of AL. As in several previous studies, high AL was defined as a score greater than or equal to 4, and low AL as a score less than 4 [5,17,18]. We performed additional sensitivity analyses using a high/low cutoff of 3, and categorizing AL as high (4+), moderate (2–3), or low (0–1), with similar results.

Statistical analysis

The complex survey design procedures in SAS 9.2 (SAS, Inc., Cary, NC) were used for statistical analysis. NHANES provides sample weights that account for nonresponse, stratification, and clustering. Subsamples of NHANES data require special weighting; this study combined laboratory subsample weights for 1999 through 2006. These weights were modified to account for the differing age distributions of pregnant and nonpregnant women. Age standardization was based on the birth rates for women in different age and race categories.

The significance of demographic variables and mean levels of AL-related biomarkers were assessed using independent two-sided *t*-tests for continuous variables and χ^2 tests for categorical variables. Because AL is an ordinal variable and is not normally distributed, the Wilcoxon rank-sum test was used to compare the distributions of AL scores. Logistic regression models were used to assess sociodemographic factors as predictors of high AL. The significance level was not adjusted for multiple comparisons.

Human subject protections

This study was approved by the Institutional Review Board of the University of Maryland in College Park.

Results

Demographics of pregnant and nonpregnant women in NHANES

Pregnant women were younger and more likely to be married than nonpregnant women ($P < .01$; Table 1). Pregnant women were also less likely to be non-Hispanic white and more likely to be non-Hispanic black or Mexican American than nonpregnant women ($P < .01$). There was no difference in education level or ratio of family income to poverty between the pregnant and nonpregnant women ($P = .16$ for education; $P = .21$ for income).

Assessing AL in pregnant and nonpregnant women

As anticipated, the mean level of each AL-related biomarker differed significantly between pregnant and nonpregnant women ($P < .01$; Table 1). AL scores were also significantly different: Pregnant women had a median AL score of 3, whereas nonpregnant women had a median AL score of 2 ($P < .01$). Both groups had a mean AL score of 2.75, and the scores followed a similar distribution.

AL and sociodemographic factors

Logistic regression models using age-standardized weights predicted the likelihood of having high AL with regard to race, age, income, and education level (Table 2). Among both the pregnant and nonpregnant women, race was significantly associated with AL, but the pattern of findings differ. In nonpregnant women, non-Hispanic blacks had greater odds of having high AL than non-Hispanic whites ($P < .01$). However, among pregnant women non-Hispanic blacks seemed to have a lower risk of high AL than non-Hispanic whites, although the difference was not significant ($P = .07$). Pregnant women who were Mexican American were less likely to have high AL than non-Hispanic white women ($P < .01$), a finding that was not significant in the nonpregnant women ($P = .08$).

Among pregnant women, the odds of having high AL did not differ by age ($P = .65$) or income ($P = .42$). Having a high school level of education, but not greater than high school, was associated with a lower likelihood of having high AL compared with less than high school ($P = .02$). Among nonpregnant women, the odds of having high AL increased with age starting with the 25- to 29-year-old age group and decreased with increasing income, particularly in the highest income groups. However, education level was not associated with the odds of having high AL in for any level of education in nonpregnant women ($P = .88$).

Discussion

The meaningfulness of measuring AL during pregnancy has not been well studied, because it is challenging to differentiate the effects of chronic stress from the changes that occur as a normal part of pregnancy. We address this important research question by assessing the attributes of AL in a nationally representative sample of pregnant and nonpregnant women. Previous studies of AL in nonpregnant populations have determined that AL increases with age and is higher among blacks than among whites [5,9,19,20]. AL also tends to be higher among people of lower socioeconomic status (income and education levels) [9,19]. We hypothesized that, if AL measured during pregnancy represents a woman's true AL, it would have similar attributes in pregnant and nonpregnant women.

Normal physiologic changes associated with pregnancy clearly impact AL scoring [10]. The distributions of AL differed significantly between U.S. pregnant and nonpregnant women. In addition, AL did not have the expected sociodemographic associations during pregnancy. The results for nonpregnant women were consistent with those of previous studies (e.g., higher AL among women who are black, are older, and have lower incomes). However, among pregnant women, the proportion of high AL actually seemed to be somewhat lower among non-Hispanic blacks compared with non-Hispanic whites. Furthermore, no differences in the proportion of high AL were noted in pregnant women of different ages, incomes, or education levels.

Our results are consistent with those of Wallace and Harville [8], who found that AL, measured using five biomarkers, did not follow hypothesized patterns in their exploratory study of 42 pregnant women. They also found no increase in AL with age and found significantly lower AL among blacks compared with whites. Interestingly, earlier gestational age was observed with increasing AL levels in this small study.

Because NHANES data are cross-sectional, we were unable to assess the relationship between AL during pregnancy and adverse birth outcomes. However, strengths of our study included its large, nationally representative sample and its comparisons of AL in pregnant and nonpregnant women. Our results and those of Wallace and Harville [8] suggest that the various biomarkers that comprise AL may reflect proximal factors in pregnancy more strongly than they represent exposure to chronic stress over a woman's lifetime. Therefore, our approach to measuring AL may not provide meaningful information about chronic stress in pregnant women without further consideration of pregnancy-related factors. The results of the current study raise several interesting questions about AL and pregnancy that could be addressed in future studies, particularly a longitudinal analysis that compares each individual's AL score before, during, and after pregnancy.

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Table 1

Demographics and AL scores for pregnant and nonpregnant women in NHANES, 1999–2006

	Nonpregnant women	Pregnant women	<i>P</i>
n	4993	1138	
Mean age (SE)	30.57 (0.17)	27.39 (0.32)	<.01 *
Race			<.01 *
Non-Hispanic white	66.13%	56.43%	
Non-Hispanic black	12.55%	14.22%	
Mexican American	9.43%	16.14%	
Other	11.89%	13.20%	
Education			.16
Less than high school	23.60%	22.44%	
High school diploma	22.98%	18.97%	
More than high school	53.42%	58.58%	
Marital status			<.01 *
Married	44.90%	64.27%	
Widowed	<1%	<1%	
Divorced	7.28%	<1%	
Separated	3.80%	1.84%	
Never married	35.45%	20.85%	
Living with partner	8.57%	12.08%	
Ratio of family income to poverty	2.74	2.62	.21
Means and cutoffs for AL-related biomarkers [†]			
C-reactive protein (mg/dL)			
Mean (SE)	0.41 (0.02)	0.78 (0.06)	<.01 *
Cutoff	>0.45	>0.91	
Albumin (g/dL)			
Mean (SE)	4.27 (0.01)	3.60 (0.02)	<.01 *
Cutoff	<4.01	<3.21	
Total cholesterol (mg/dL)			
Mean (SE)	186.70 (0.73)	213.24 (2.65)	<.01 *
Cutoff	>207.85	>244.51	
High-density lipoprotein cholesterol (mg/dL)			
Mean (SE)	55.70 (0.38)	64.38 (0.99)	<.01 *
Cutoff	<44.15	<51.48	
Creatinine (μmol/L)			
Mean (SE)	63.49 (0.27)	48.22 (0.79)	<.01 *
Cutoff	>70.71	>53.03	
Hemoglobin A1C (%)			
Mean (SE)	5.18 (0.01)	4.95 (0.02)	<.01 *

	Nonpregnant women	Pregnant women	<i>P</i>
Cutoff	>5.26	>5.10	
Homocysteine (μmol/dL)			
Mean (SE)	6.90 (0.06)	4.44 (0.06)	<.01 [*]
Cutoff	>7.65	>5.07	
Systolic BP (mmHg)			
Mean (SE)	111.00 (0.23)	108.34 (0.62)	<.01 [*]
Cutoff	>117.32	>113.68	
Diastolic BP (mm Hg)			
Mean (SE)	68.50 (0.27)	59.60 (0.62)	<.01 [*]
Cutoff	>74.43	>66.22	
60-second pulse rate			
Mean (SE)	75.88 (0.24)	85.76 (0.50)	<.01 [*]
Cutoff	>82.21	>92.90	
Median AL score	2	3	<.01 [*]
Mean AL score	2.75	2.75	
Range of AL scores	0–10	0–8	
Proportion with high AL (AL score >4)	30.44%	31.47%	

AL = allostatic load; BP = blood pressure; SE = standard error.

^{*} $P < .01$.

[†] Cutoff represents the high-risk quartile based on the distribution of each sample.

Table 2

Age-standardized logistic regression models for sociodemographic factors as predictors of high AL in pregnant and nonpregnant women in NHANES, 1999–2006

	Nonpregnant women[†]		Pregnant women	
	Odds ratio estimate	95% Wald confidence limits	Odds ratio estimate	95% Wald confidence limits
Race				
NH white	1.00 (ref)	—	1.00 (ref)	—
NH black	2.43	1.86, 3.18*	0.57	0.31, 1.05
MA	0.72	0.49, 1.04	0.32	0.13, 0.75*
Other	0.64	0.43, 0.95	1.61	0.67, 3.87
Age (yrs)				
15–19	1.00 (ref)	—	1.00 (ref)	—
20–24	0.79	0.69, 1.51	0.58	0.25, 1.33
25–29	1.70	1.19, 2.44*	0.65	0.30, 1.43
30–34	2.36	1.72, 3.24*	0.88	0.34, 2.27
35–44	2.80	2.08, 3.78*	0.85	0.32, 2.25
Income (ratio I/P)				
0–1.00	1.00 (ref)	—	1.00 (ref)	—
1.01–2.00	0.79	0.53, 1.20	0.73	0.30, 1.75
2.01–3.00	0.82	0.59, 1.13	0.42	0.15, 1.19
3.01–4.00	0.64	0.42, 0.97*	0.90	0.34, 2.39
4.01–5.00	0.64	0.42, 0.97*	0.51	0.18, 1.43
Education				
<HS	1.00 (ref)	—	1.00 (ref)	—
HS or equivalent	0.98	0.70, 1.37	0.33	0.12, 0.86*
>HS	0.91	0.61, 1.36	0.49	0.21, 1.16

HS = high school; I/P = family income to poverty; MA = Mexican American; NH = non-Hispanic.

* $P < .01$.

[†] The weights used for the analysis of nonpregnant women have been age standardized to reflect the age distribution of pregnant women.