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Allostatic Load and Birth Outcomes Among White and Black Women in New Orleans

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Abstract

Objectives—As a marker of chronic stress, allostatic load has been theoretically recognized as a potential contributor to racial disparities in birth outcomes. The purpose of this investigation was to identify associations between allostatic load and birth outcomes and to assess differences in allostatic load and its relation to birth outcomes between white and black women.

Methods—Blood samples from 123 women at 26–28 weeks gestation were assayed for cholesterol, glycosylated hemoglobin, dehydroepiandrosterone-sulfate, and cortisol, with 42 women having complete data on all biomarkers and birth outcomes. Together with systolic blood pressure, these biomarkers were combined to create an allostatic load index. Multiple linear regression models were used to evaluate associations between allostatic load index and gestational age, birth weight, birth weight ratio, birth length, and head circumference.

Results—Black women had a significantly lower allostatic load index than white women ($P < 0.05$). Gestational age was the only outcome significantly associated with allostatic load in both unadjusted and adjusted models ($P < 0.05$). Gestational age decreased significantly with increasing allostatic load (adjusted β : -0.18 , 95% CI: -0.35 , 0.00). A significant interaction with age indicated that the effect was less strong at higher maternal ages (adjusted interaction β : 0.04 , 95% CI: 0.00 , 0.08). There was no racial difference in the effect of allostatic load on birth outcomes.

Conclusions—These findings represent possible evidence of the effect of stress age on gestational age. As a measure of cumulative disadvantage, allostatic load may prove to be a contributor to the racial disparities in birth outcomes.

Keywords

Allostatic load; Stress; Pregnancy; Birth outcomes

INTRODUCTION

The concepts of allostasis and allostatic load provide a framework through which to evaluate the impact of cumulative burden across the life course that places some women at increased risk for adverse birth outcomes even before pregnancy (1). Allostasis refers to the body's dynamic process of physiologic regulation and adaptation in response to stress (2), while allostatic load is the dysregulation of the stress response process; it is the “wear and tear” on the body that arises from chronic, prolonged or persistent activation of allostatic effectors and a breakdown of the regulatory feedback mechanisms (2, 3). When threatened by

adversity (real or perceived), activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to a cascade of physiologic events involving cardiovascular, metabolic, immune, and neuroendocrine system effectors that promote protection and adaptation and allow the body to maintain physiologic stability. Specifically, HPA-released hormones act to increase heart rate and blood pressure, promote glucose production, and ready important immune cells, collectively enabling a “fight or flight” behavioral response to stress (3, 4). Once the threat or stressor is removed, dynamic feedback mechanisms turn off the response pathways, allostatic effectors return to a lowered physiologic level, and the body is restored to an apparent steady state (5). However, under chronic stress this wear and tear or “weathering” essentially accelerates biologic aging such that individuals with a high allostatic load experience increased vulnerability to stress-related disease and an earlier decline in overall health compared to their counterparts of the same chronologic age (2, 6).

Allostatic load has been posited as a potential contributor to adverse birth outcomes, particularly in those cases that lack more readily apparent biologic risk factors (7, 8). As a marker of weathering or stress age, it follows that allostatic load would be associated with adverse birth outcomes known to increase with maternal age and would be higher in groups at higher risk of adverse outcomes (9). The lowest risk age group for preterm birth among non-Hispanic white women is 30–34, while for black women it is 25–29, such that the age-associated increase has been shifted younger (10). Black women also show a steeper and earlier age-related rise of risk for term small-for-gestational-age (11). Yet despite the strong theoretic plausibility and the fact that it is frequently proposed as a hypothesis to explain racial disparities (7, 8, 12–16), to our knowledge allostatic load has not been directly studied with respect to pregnancy. The purpose of this investigation was to identify associations between allostatic load and birth outcomes and to assess the differences, if any, in allostatic load and its relation to birth outcomes between white and black women.

METHODS

Subject Recruitment

Women were recruited for participation at Tulane-Lakeside Hospital Department of Obstetrics and Gynecology during a prenatal care visit between 20 and 30 weeks gestation. Eligible women were between ages 20 and 35 with a singleton pregnancy, self-identified as white or African-American, English speaking, and receiving prenatal care with planned delivery at Tulane-Lakeside Hospital. After obtaining informed consent, women were asked to complete a brief questionnaire including demographic, behavioral, and medical history information. This study and all data collection materials were approved by the Tulane University Institutional Review Board.

Exposure Measurement

During the routinely scheduled glucose tolerance test (26–28 weeks’ gestation), an additional 15 mL blood was drawn by hospital laboratory phlebotomists for study purposes. Studies have utilized composite measures of allostatic load ranging from 5 up to 17 biomarkers from cardiovascular, neuroendocrine, immune, and metabolic systems and anthropometric indicators (17). For this study, allostatic load component biomarkers measured included cholesterol, glycosylated hemoglobin (HbA1c), dehydroepiandrosterone-Sulfate (DHEA-S), cortisol, and systolic blood pressure, representing metabolic, neuroendocrine, and cardiovascular systems, respectively. Time-sensitive assays for cholesterol, DHEA-S, and HbA1c were performed immediately by trained laboratory technicians. Remaining serum was frozen until study recruitment ended, at which time a random sample of 42 stored sera (the maximum number study funding would allow) were assayed for cortisol at the downtown Tulane University Hospital lab. Cholesterol and

HbA1c assays were performed using the Siemens Dimension Vista System®. Cortisol levels in thawed samples were measured via the Siemens Centaur Cortisol assay and DHEA-S via the Electrochemiluminescence Immunoassay (ECLIA). Blood pressure at prenatal care visits was obtained from each woman's medical record.

Outcome Measurement

Abstraction of medical records provided detailed information on reproductive history and the course of pregnancy, labor, and delivery. Self-reported tobacco use, parity, and pre-pregnancy weight were obtained from medical records. Infant delivery records were abstracted for birth outcome variables including gestational age at delivery, birth weight, birth length, and head circumference. Birth weight ratio was computed by dividing birth weight in grams by the mean birth weight for gestational age.

Statistical Analysis

Racial differences in biomarker levels and birth outcomes were assessed in bivariate analysis using t-tests for independent samples among all women with individual biomarker data available. Cortisol measurements were standardized relative to the sample mean at the time of day blood was drawn. The remaining biomarkers (cholesterol, cortisol, DHEA-S, HbA1c, and systolic blood pressure at the earliest prenatal care visit with available data) were standardized relative to their distribution in the total sample. An allostatic load index for each woman was then computed by summing z-scores for all five biomarkers. At least 12 different algorithmic computations of allostatic load have been cited in the literature (17). We chose to utilize the z-score method because it allows the weight to vary with relation to the deviation of each biomarker from the sample mean, in our view important flexibility given the inherently altered physiologic state of pregnancy.

Multiple linear regression models were used to evaluate associations between allostatic load index and infant outcomes among women with complete data on all five allostatic load biomarker components (n=42). Tests for two- and three-way interactions with age (continuous) and race were also conducted. Age was centered at the mean to facilitate interpretation. Adjusted models included pre-pregnancy BMI and smoking during pregnancy as potential confounding covariates.

RESULTS

Three of the five allostatic load biomarkers differed significantly between white and black women (Table 1). Cholesterol and cortisol were higher among white women compared to black women, while black women had higher HbA1c (all $P < 0.01$). Contrary to the study hypothesis, black women had a significantly lower combined allostatic load index than white women. Mean birth length and head circumference were both larger among infants born to white mothers compared to black, and there was no significant racial difference in mean gestational age at delivery or birth weight in our sample.

When the components of the allostatic load index were examined individually, only cholesterol was significantly and positively associated with birth length (β : 0.02, 95% CI: 0.001, 0.03; table 2). Increasing allostatic load appeared to increase birth weight, birth weight ratio, birth length, and head circumference, though the relationships were not significant (all $P > 0.10$; table 3). Gestational age was the only outcome significantly associated with allostatic load in both unadjusted and adjusted models ($P < 0.05$). As hypothesized, the relationship appeared inverse such that gestational age decreased significantly with increasing allostatic load (adjusted β : -0.18, 95% CI: -0.35, 0.00); likewise, increasing age decreased gestational age, though the relationship in this sample

was not significant. The significant positive two-way interaction indicates that the effect of allostatic load on gestational age was less strong at higher ages ($P<0.05$). Adjustment for maternal age and body mass index had little effect on the coefficient estimates.

DISCUSSION

Our preliminary investigation sought to identify differences in allostatic load among black and white pregnant women and to understand how maternal allostatic load might impact birth outcomes of the infant. Literature on non-pregnant populations has associated allostatic load with peripheral arterial disease, diabetes, and other multi-systemic disease etiologies (17). In older adults, allostatic load is thought to lead to neuroendocrine changes, vulnerability to infection or inflammation, and increased risk of cardiovascular complications such as hypertension and diabetes (7). Racial/ethnic differences in allostatic load resulting from persistent experiences of racism, poverty, educational disadvantage, and perceived stress and anxiety may account for the increased rates of these adverse health outcomes observed among blacks in the US (18). Black women in particular have been shown to have higher mean allostatic load compared to black males and white males and females (18, 19), a disparity which – like that of preterm birth – exists independent of socioeconomic status (20).

Among pregnant women, acute and chronic stress has been associated with the occurrence of preterm birth and low birth weight; however, research has been limited by inconsistent and incomplete measures of chronic stress in particular (12). While individually the physiological consequences of allostatic load such as high blood pressure, metabolic dysfunction, and diabetes are known risk factors for preterm birth, (21, 22), to our knowledge the collective and multisystemic impact of allostatic load has not been studied with respect to birth outcomes. In our data, gestational age was the only birth outcome of those investigated that appeared to be affected by allostatic load. While there was no evidence of a differential effect by race, it nonetheless represents possible evidence of weathering or the effect of stress age (7) on gestational age in our small sample. Allostatic load appeared to increase with increasing age overall, though the association was not significant (data not shown). Besides gestational age, there was no evidence of a relationship between allostatic load and the remaining birth outcomes investigated.

Key to the allostatic load model is collective action of component biomarkers, which has been shown to be more uniformly predictive than individual biomarkers or single-system clusters, particularly with regard to longer-term outcomes and physical functioning (23). However, the multiple cross-systems interactions and non-linear effects of stress response mediators have made the quantification and operationalization of allostatic load difficult. A recent review summarized the literature on allostatic load and the variety of approaches to establishing a composite, quantifiable definition (17). Studies have utilized composite measures of allostatic load ranging from 5 up to 17 biomarkers from cardiovascular, neuroendocrine, immune, and metabolic systems and anthropometric indicators (17). A factor analysis of biomarker clusters revealed a promising “metafactor” model of allostatic load comprised of six independent subfactors: heart rate variability, blood pressure, inflammation markers, metabolic parameters, cortisol, and sympathetic nervous system hormone markers (19). Allostatic load in the current study utilized markers from four of the six subfactors. Future research should incorporate more of these markers.

The limitation of our small sample size prohibits drawing definite conclusions. There was no significant difference in birth weight or gestational age between white and black women in our sample, and as such it does not mirror the disparity in our state population. Likewise, our ability to detect the impact of allostatic load and its magnitude in contribution to the

disparity may have been underpowered. Study funding prohibited further serum assays which would have increased our sample size and power. At present, however, there is no established, valid, and comprehensive measure of allostatic load (17), and our findings contribute to the discussion of potential component biomarkers, as well as providing initial evidence for the racially differential distribution of these biomarkers during pregnancy and their collective impact on birth outcomes. As a measure of cumulative burden and a physical consequence of societal disadvantage, allostatic load may yet prove to be an important contributor to the perplexing and persistent racial disparity in birth outcomes.

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References

1. Lu MC, Kotelchuck M, Hogan V, Jones L, Wright K, Halfon N. Closing the black-white gap in birth outcomes: A life-course approach. *Ethn Dis*. 2010 Winter;20(1 Suppl 2):S2, 62–76.
2. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med*. 1998 Jan 15; 338(3):171–9. [PubMed: 9428819]
3. McEwen BS. Stress, adaptation, and disease. allostasis and allostatic load. *Ann N Y Acad Sci*. 1998 May 1.840:33–44. [PubMed: 9629234]
4. McEwen BS. The neurobiology of stress: From serendipity to clinical relevance. *Brain Res*. 2000 Dec 15; 886(1–2):172–89. [PubMed: 11119695]
5. Goldstein DS, McEwen B. Allostasis, homeostats, and the nature of stress. *Stress*. 2002 Feb; 5(1): 55–8. [PubMed: 12171767]
6. McEwen BS, Wingfield JC. The concept of allostasis in biology and biomedicine. *Horm Behav*. 2003 Jan; 43(1):2–15. [PubMed: 12614627]
7. Hogue CJ, Bremner JD. Stress model for research into preterm delivery among black women. *Am J Obstet Gynecol*. 2005 May; 192(5 Suppl):S47–55. [PubMed: 15891712]
8. Shannon M, King TL, Kennedy HP. Allostasis: A theoretical framework for understanding and evaluating perinatal health outcomes. *J Obstet Gynecol Neonatal Nurs*. 2007 Mar-Apr;36(2):125–34.
9. Geronimus AT. Black/white differences in the relationship of maternal age to birthweight: A population-based test of the weathering hypothesis. *Soc Sci Med*. 1996 Feb; 42(4):589–97. [PubMed: 8643983]
10. Rich-Edwards JW, Grizzard TA. Psychosocial stress and neuroendocrine mechanisms in preterm delivery. *Am J Obstet Gynecol*. 2005 May;192:S30–S35. [PubMed: 15891710]
11. Ananth CV, Balasubramanian B, Demissie K, Kinzler WL. Small-for-gestational-age births in the United States: an age-period-cohort analysis. *Epidemiology*. 2004; 15:28–35. [PubMed: 14712144]
12. Latendresse G. The interaction between chronic stress and pregnancy: Preterm birth from a biobehavioral perspective. *J Midwifery Womens Health*. 2009 Jan-Feb;54(1):8–17. [PubMed: 19114234]
13. Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: A life-course perspective. *Matern Child Health J*. 2003 Mar; 7(1):13–30. [PubMed: 12710797]
14. Tiedje LB. Psychosocial pathways to prematurity: Changing our thinking toward a lifecourse and community approach. *J Obstet Gynecol Neonatal Nurs*. 2003 Sep-Oct;32(5):650–8.

15. Morello-Frosch R, Shenassa ED. The environmental “riskscape” and social inequality: Implications for explaining maternal and child health disparities. *Environ Health Perspect*. 2006 Aug; 114(8):1150–3. [PubMed: 16882517]
16. Power ML, Schulkin J. Maternal obesity, metabolic disease, and allostatic load. *Physiol Behav*. 2011 Sep 14.
17. Juster R, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience & Biobehavioral Reviews*. 2010; 9;35(1):2–16.
18. Geronimus AT, Hicken M, Keene D, Bound J. “Weathering” and age patterns of allostatic load scores among blacks and whites in the united states. *Am J Public Health*. 2006 May; 96(5):826–33. [PubMed: 16380565]
19. Seeman T, Gruenewald T, Karlamangla A, Sidney S, Liu K, McEwen B, et al. Modeling multisystem biological risk in young adults: The coronary artery risk development in young adults study. *Am J Hum Biol*. 2010 Jul-Aug;22(4):463–72. [PubMed: 20039257]
20. Love C, David RJ, Rankin KM, Collins JW Jr. Exploring weathering: Effects of lifelong economic environment and maternal age on low birth weight, small for gestational age, and preterm birth in african-american and white women. *Am J Epidemiol*. 2010 Jul 15; 172(2):127–34. [PubMed: 20576757]
21. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008 Jan 5; 371(9606):75–84. [PubMed: 18177778]
22. Chappell LC, Enye S, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: A prospective study. *Hypertension*. 2008 Apr; 51(4):1002–9. [PubMed: 18259010]
23. Seeman TE, McEwen BS, Rowe JW, Singer BH. Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging. *Proc Natl Acad Sci U S A*. 2001 Apr 10; 98(8):4770–5. [PubMed: 11287659]

Table 1
Frequencies of Allostatic Load Components, Allostatic Load Index, Covariates, and Birth Outcomes by Race

Variable	Total			Black			White		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Allostatic Load Biomarkers									
Cortisol **	42	17.2	5.7	21	14.8	5.03	21	19.5	5.4
Cholesterol **	122	233.6	43.8	63	222.7	42.1	59	245.3	42.8
DHEA-S	123	117.6	81.5	64	112.5	64.8	59	123.2	96.6
Glycosylated hemoglobin **	87	5.5	0.5	47	5.7	0.5	40	5.3	0.3
Systolic blood pressure	110	110.7	11.0	58	111.5	12.1	52	109.9	9.6
Allostatic Load Index *	31	0.2	1.7	16	-0.5	1.7	15	0.9	1.5
Age	120	26.7	4.3	64	26.1	4.3	56	27.5	4.3
BMI	120	27.2	8.9	63	29.8	10.0	57	24.3	6.5
Birth Outcomes									
Gestational age, weeks	120	38.9	1.5	61	39.0	1.3	59	38.7	1.7
Birth weight, grams	122	3327.8	458.9	63	3288.8	459.9	59	3369.4	458.0
Birth weight Ratio	119	1.0	0.2	60	1.00	0.1	59	1.0	0.3
Birth length, cm *	122	50.2	3.7	64	49.4	3.2	58	51.0	4.1
Head circumference, cm **	85	33.8	2.5	42	33.1	2.8	43	34.5	1.9

* $P < .05$ (t-test difference in means)

** $P < 0.01$

Table 2

Unadjusted Mean Difference in Birth Outcome by Allostatic Load Index Components

Component	Birth weight ratio		Gestational age, wks		Birth weight, g		Birth length, cm		circumference, cm Head	
	β	95% CI	β	95% CI	β	95% CI	B	95% CI	β	95% CI
Cortisol	0.01	-0.01 0.03	-0.06	-0.17 0.04	-10.10	-35.40 15.21	-0.17	-0.42 0.07	0.14	-0.05 0.33
Cholesterol	0.0008	-0.0001 0.002	-0.002	-0.01 0.004	1.07	-0.81 2.95	0.02	0.001 0.03*	0.003	-0.01 0.02
DHEA-S ^a	0.03	-0.03 0.09	-0.18	-0.58 0.22	10.93	-111.05 132.91	-0.69	-1.66 0.29	-0.04	-0.80 0.73
HsCRP	-0.06	-0.17 0.06	0.24	-0.48 0.96	50.50	-168.44 269.43	-0.39	-2.28 1.50	0.06	-1.40 1.52
SBP	0.001	-0.0004 0.004	-0.01	-0.03 0.01	5.81	-1.88 13.49	0.02	-0.03 0.07	-0.02	-0.0 0.03

* $P < 0.05$ ^a Log-transformed

Table 3
Unadjusted and Adjusted Linear Regression Models for Mean Difference in Birth Outcomes by Allostatic Load Index

Outcome	Predictor(s)	Unadjusted			Adjusted ^a		
		β	95% CI	P	β	95% CI	P
Birth weight, grams	Allostatic load	50.59	-52.48 153.66	0.34	50.60	-55.95 142.40	0.39
Birth weight ratio	Allostatic load	0.02	-0.01 -0.05	0.13	0.02	-0.01 0.05	0.16
Birth length, cm	Allostatic load	0.32	-0.14 0.78	0.17	0.31	-0.13 0.75	0.16
Head circumference, cm	Allostatic load	0.43	-0.34 1.19	0.27	0.37	-0.40 1.15	0.34
Gestational age, weeks ^b							
	Allostatic load	-0.17	-0.35 0.00	0.05	-0.18	-0.35 0.00	0.05
	Age ^c	-0.02	-0.10 0.06	0.62	-0.03	-0.11 0.05	0.46
	Allostatic load*age	0.04	0.01 0.08	0.02	0.04	0.00 0.08	0.03

^a All models adjusted for smoking and body mass index.

^b Significant allostatic load by age interaction retained in the model ($P < 0.05$)

^c Age centered at the mean.