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Acknowledging and Addressing Allostatic Load in Pregnancy Care

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Abstract

The U.S. is one of the few countries in the world in which maternal and infant morbidity and mortality continues to increase, with the greatest disparities observed among non-Hispanic Black women and their infants. Traditional explanations for disparate outcomes, such as personal health behaviors, socioeconomic status, health literacy, and access to healthcare do not sufficiently explain why non-Hispanic Black women continue to die at three to four times the rate of White women during pregnancy, childbirth, or postpartum. One theory gaining prominence to explain the magnitude of this disparity is allostatic load, or the cumulative physiological effects of stress over the life-course. People of color disproportionately experience social, structural, and environmental stressors that are frequently the product of historic and present-day racism. In this essay we present the growing body of evidence implicating the role of elevated allostatic load in adverse pregnancy outcomes among women of color. We argue that there is a moral imperative to assign additional resources to reduce the effects of elevated allostatic load before, during, and after pregnancy to improve the health of women and their children.

Keywords

allostatic load; weathering hypothesis; maternal morbidity and mortality; infant morbidity and mortality; health disparities

Introduction

The United States has the undesirable distinction of being the only nation in the Organization for Economic Cooperation and Development in which maternal and infant morbidity and mortality have not only failed to decline but are actively rising. These deaths

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are disparately seen among women and infants of color. Non-Hispanic Black women experience three to four times the maternal mortality rate of non-Hispanic White women and are more than twice as likely as non-Hispanic White women to experience severe maternal morbidity that may contribute to mortality later in life [1–3]. American Native and Indigenous women also experience markedly elevated risk levels for maternal mortality and morbidity while Hispanic women experience elevated rates, although less significant. In addition to increased maternal mortality and morbidity, ethnic minority populations experience higher rates of adverse fetal and neonatal outcomes. These outcomes include preterm birth, fetal growth restriction, congenital abnormalities, and fetal demise [4]. While overall rates of infant mortality have fallen steadily in the past few decades, infants born to non-Hispanic Black women continue to die at more than twice the rate of non-Hispanic White infants [5, 6]. By one estimate, complications arising from preterm birth/low birthweight account for approximately 80% of this disparity in neonatal mortality [7].

Traditional Factors in Maternal-Fetal Outcomes

Historic understandings of disparities in maternal-fetal outcomes focused primarily on health behaviors and access to quality medical care. Public health officials frequently cited socioeconomic status, single parenthood, and health conditions such as obesity, hypertension, poor nutrition, and controlled substance use as causes of disparate outcomes. States also focused on factors related to access to care, such as Medicaid coverage, during pregnancy. Expanded income eligibility for Medicaid during pregnancy is now policy in 37 states [8]. However, as monitoring of maternal-fetal outcomes improved and expanded to cover populations other than Medicaid patients, it became increasingly clear that these traditional explanations failed to account for the magnitude of the disparities. For example, a recent statistical analysis found that socioeconomic status accounted for only 21.4% of the racial gap in low birthweight and 19% of the difference in preterm birth [9]. In populations with equal access to quality healthcare, such as members of the U.S. military, racial disparities in pregnancy outcomes are reduced but not eliminated. Non-Hispanic Black women receiving military medical care are still at increased risk for low birthweight, preterm birth, and placental abruption, implicating the role of additional factors in poor maternal-fetal outcomes among women of color [10–14]. Even now, as the scope of the disparity is increasingly clear, many states do not have systematic registries that may elucidate such factors and explain increasing maternal morbidity and mortality.

At every education and income level, non-Hispanic Blacks encounter higher morbidity and mortality than any other ethnic group [15]. Indeed, non-Hispanic Black women with graduate degrees have higher rates of severe maternal morbidity than non-Hispanic White women who never graduated from high school [16]. Moreover, while non-Hispanic White women experience a protective benefit against adverse birth outcomes with increased socioeconomic status, this advantage is not observed among non-Hispanic Black women [17, 18]. More favorable birth outcomes are also observed among foreign-born Black and less acculturated women, despite the fact that these groups typically have lower socioeconomic status [19–23]. This suggests that neither health literacy, access to health insurance, nor standards of health care account for existing disparities.

Other individual risk factors, such as increased prevalence of hypertensive disease, obesity, and diabetes in minority women prior to pregnancy, also do not explain the magnitude of disparities [24–26], nor do they explain why women of color are more likely to die than non-Hispanic White women with the same pregnancy risk-factors [27]. Similarly, alcohol consumption during pregnancy is very slightly elevated in non-Hispanic Black women when compared to non-Hispanic White women [28] and smoking during pregnancy is markedly lower in Hispanic women compared to non-Hispanic White women [29]. Yet these health behaviors do not correspond with increased morbidity among non-Hispanic White women. Individual genetics also do not account for the significantly increased risk of preterm birth among non-Hispanic Black women; while certain genetic polymorphisms have been identified, their cumulative effect is small [30, 31]. Additionally, while one study found that 35.2% of variation in gestational age at birth in European Americans could be explained by fetal genetic factors, this was true for only 3.7% of African-Americans. In contrast, variance in gestational age at birth for African-American was twice that of European Americans, and 82.5% of this variance was attributed to environmental factors [32].

Allostatic Load as an Explanation for Maternal-Fetal Disparities

It appears, therefore, that traditional risk factors related to individual behavior and socioeconomic status do not fully explain racial differences in reproductive outcomes [15, 33]. Alternative explanations, including potential psychosocial and environmental mechanisms are the subject of ongoing research. This research focuses on structural factors that impact not only individual behaviors or access – i.e. whether one individual mother complies with folic acid supplementation or attends multiple prenatal clinic visits – but the systemic forces that may affect outcomes on a population level. One theory gaining increasing attention is the idea of allostatic load, or the cumulative psychological and physiological impact of stress over the life-course. Allostatic load provides a plausible biological mechanism that may explain how even wealth and “proper” health behaviors fail to insulate certain groups of women against risk in pregnancy and childbirth. Illustrating this, a recent study used hierarchical clustering to analyze stressful life events preceding delivery in a population of pregnant women, resulting in three different stressor landscape groups: a protected stressor landscape, isolated stressor landscape, and toxic stressor landscape. The stressor landscapes have differential impact depending on race and income. A high income was found to be protective for White women, but not for Black and Hispanic women. Indeed, the greatest racial disparities were observed among upper middle-class women [34]. According to the model of allostatic load, the constant and omnipresent stress of experiencing and combatting discrimination and inequality tied to gender and race contributes to metabolic conditions that exacerbate existing pregnancy-related risks, including preterm birth and other factors that contribute to infant health [35]. In contrast to models relying on traditional factors, allostatic load explains the paradoxical findings that pregnancy outcomes worsen with increasing education and socioeconomic status among women of color, especially since upward mobility is associated with increased exposure to acute and chronic discrimination [36]. Differential exposure to stress across the lifetime may thus explain why minority populations suffer from poorer longitudinal health and higher mortality rates, including increased adverse maternal and neonatal outcomes [35].

Allostasis is the process of maintaining homeostasis in response to environmental stressors, including dynamic changes in neuroendocrine and immune system activity. Physiological responses to stress include intensifying the activity of the hypothalamic-pituitary-adrenal (HPA) axis to increase heart rate, blood pressure, and glucose production and altering immune system activity to prepare the body for a “fight or flight” response. Once the stressor is removed, these systems return to baseline. These changes are intended to protect the body from immediate harm, but when repeated or sustained inflict long-term damage [37, 38]. Allostatic load, as coined by McEwen and Stellar in 1993 [39], describes the cumulative “wear and tear” inflicted on the body in response to external stressors [40]. Elevated and sustained HPA activity disrupts the balance of the immune system and leads to inflammation, the common culprit in stress-related diseases [41]. Repeated stress burden may also lead to a reduced ability to physiologically adapt or shut down allostatic responses, preventing the ability to withstand future stressors [37].

Allostatic load is measured by several neuroendocrine, metabolic, cardiovascular, and inflammatory biomarkers that shift in response to a dysregulated stress response [38]. This results in several clinical outcomes, including hypertension, cardiovascular disease, and metabolic syndrome, all of which complicate pregnancy. Several studies have identified correlations between elevated allostatic load and risk of preterm birth, low birthweight, and pre-eclampsia[42–46]. As parturition is marked by a shift from anti-inflammatory to pro-inflammatory pathways to initiate uterine contractility, membrane rupture, and placental detachment, this suggests elevated inflammation during pregnancy due to high allostatic load may increase risk of preterm birth [47, 48]. Allostatic load may also be inherited; animal studies have demonstrated the transgenerational inheritance of epigenetic changes resulting from stress exposure [49]. One study found the length of gestation was progressively reduced in subsequent generations following maternal exposure to prenatal stress [50]. Assuming these models translate to humans, women of color may have a unique vulnerability to pregnancy complications due to epigenetic predisposition of the racial discrimination experienced by prior generations, as well as a dysregulated stress response from chronic exposure to environmental stressors.

Given the scientific evidence for the effects of elevated allostatic load on pregnancy outcomes, and thus directly on patient well-being, we argue that there is a moral imperative to assign significant resources towards reducing allostatic load on patients and society in general, and in the healthcare setting specifically. This is especially the case since the evidence thus far suggests addressing traditional factors, such as individual health behaviors, will not meaningfully reduce racial disparities in health outcomes. Focusing only on patient rather than systemic factors also fails to take sufficient accountability for past and present injustices including differential treatment and discrimination based on race. Here, we will first expand on the evidence for the explanatory factor of allostatic load in prenatal and perinatal outcomes and argue that a commitment to principles of social justice calls for greater attention to the role of racism and elevated allostatic load in adverse pregnancy outcomes.

Allostatic Load and Race

Various social, structural, and environmental stressors disproportionately burden people of color. Several studies have described the unique race-related stress experienced by African Americans living in a predominantly White, racially stratified society [51–55]. This includes experiences of explicit and implicit interpersonal racism and structural racism, including racist remarks, negative interactions with law enforcement, unfair treatment by service industry employees, and lower pay than White coworkers [56–63]. In addition, women of color experience the impact of gender discrimination, sexual harassment, and sexism as well as race-related discrimination, suggesting the accumulation of stress over the life-course is intersectional. Out of all demographic groups, black women have the highest documented allostatic load scores [64–67].

Structural racism results in inequalities in power, access, treatment quality, and opportunities. Many American cities remain geographically segregated despite increasing racial and ethnic population diversity [68]. These conditions are a legacy of Jim Crow laws such as the National Housing Act of 1934 that institutionalized the redlining of minority neighborhoods. The lack of financial investment in certain neighborhoods based on racial/ethnic demographics prevented minority home ownership and accelerated the decline of property values and housing deterioration and abandonment, leading to present day racial residential segregation, economic inequality, and reduced upward mobility in cities where redlining was practiced [69]. This has resulted in differential daily exposure to environmental stressors associated with fewer resources, poorer infrastructure, and higher rates of poverty, crime, and violence than exist in majority White neighborhoods [70, 71]. Residential segregation also negatively impacts health-related behaviors that may mitigate the effects of stress, such as access to healthy food and exercise as a result of urban food deserts and lack of neighborhood amenities, green spaces, and safety [72–78].

Black communities are also impacted by the mass incarceration of African American men, which further contributes to disproportionate stress [79]. Having been incarcerated or having an intimate partner who has been or is incarcerated is shown to increase a woman's risk of stress-related disease [80]. Mass incarceration may affect women uniquely by eliminating their social and financial support, as incarcerated men are unlikely or unable to contribute financially to their families [81]. Furthermore, there is a growing trend of women of color becoming incarcerated for short periods of time during pregnancy for minor civil or criminal infractions, a practice which disrupts access to healthcare, drains financial resources, and disrupts family relationships [75, 82–84]. Parent incarceration, parent death, food/housing insecurity, neighborhood violence, and racial discrimination are also known adverse childhood experiences (ACE). ACEs are more prevalent among non-Hispanic Black and Hispanic children and are associated with increased risk of poor health outcomes, including pregnancy loss and preterm birth [85–93].

Allostatic Load and Pregnancy Outcome Disparities

Allostatic load provides a framework for understanding the role of differential lifetime stress in maternal-fetal health disparities [44, 94–96]. The concept of “weathering,” first proposed

by Geronimus in 1992, has guided exploration of how chronic stress before pregnancy may contribute to birth outcome disparities. This hypothesis proposes that the cumulative effects of racism, economic disadvantage, and associated stress over a Black woman's lifetime erodes her health and puts her at higher risk for poor obstetric outcomes with increasing age [97]. While initially rooted in sociological observation, subsequent biological evidence supports the cumulative effects of racial stress over the life-course; Black women are biologically seven and a half years older than White women of the same chronological age as measured by telomere length, with perceived stress and poverty accounting for 27% of this difference [98].

Research into the role of chronic stress in preterm delivery supports the weathering hypothesis, demonstrating racial disparities in preterm birth and low birthweight that increase with maternal age, particularly for women who live in impoverished areas [99–103]. Specifically, the association between maternal stress associated with racism and socioeconomic disadvantage and a higher incidence of preterm birth/low birthweight in Black women has been repeatedly demonstrated [17, 45, 104–110]. Living in segregated and under-resourced neighborhoods is also a known factor in adverse birth outcomes [111–119]. Violent crime is the primary source of stress in many urban neighborhoods; it is also one of the most robust neighborhood-related predictors of birthweight and pregnancy complications [71, 120].

In addition to studies establishing a correlation between chronic stress during pregnancy and adverse pregnancy outcomes [121–126], a growing body of research has examined the association of allostatic load biomarkers with pregnancy outcomes. This is admittedly challenging since normal pregnancy-related physiological changes likely prevent accurate measurement of a woman's true allostatic load during pregnancy [127, 128]. Consequently, many studies must rely on allostatic load measured pre-conception or post-delivery. Timing of allostatic load measurement may be critical; one study that did not find an association between allostatic load and pregnancy outcomes relied on measurements collected on an average of 6.8 years prior to pregnancy at a mean age of 13 years [129, 130]. However, a recent study measuring allostatic load biomarkers at four months prior to pregnancy found that a unit increase in allostatic load was associated with increased odds of preeclampsia (62%), preterm birth (44%), and low birthweight (39%) [46]. A matched control study also found that in early pregnancy, higher allostatic load is associated with increasing odds of preeclampsia [131]. Using postpartum measurements, a study using National Health and Nutrition Examination Survey data found that women with a history of low birthweight or preterm birth had higher allostatic load compared to women with normal weight deliveries [132]. A second study examining allostatic load at 45 weeks postpartum found a significant association between elevated allostatic load and a composite of low birthweight, preeclampsia, preterm birth, and gestational diabetes [133]. Measurement postpartum may also not be indicative of its true value during pregnancy, as compromised maternal-fetal health and parenting stress may contribute to elevated allostatic load following delivery. Nevertheless, the data thus far indicates elevated allostatic load during pregnancy contributes to poor maternal-fetal outcomes.

Allostatic Load in Health Care and Unconscious Bias

Another major source of stress reported by women of color is in interacting with the health care system and medical personnel [134–137]. Extensive research has shown that the frequency of accessing prenatal care is significantly correlated with better birth outcomes in both mothers and infants. However, there is significant evidence that women of color access care during the prenatal period less than other women and that, when they do, they report worse experience of care, contributing to additional stress and reinforcing avoidance of care settings. These findings hold even when controlling for physical and financial barriers to care. Women of color report negative experiences of medical care across the spectrum, but particularly in reproductive and women’s health-specific care. Black women are more likely to have an inappropriate hysterectomy for uterine fibroids [138]; are recommended long-acting hormonal birth control methods despite patient preferences and symptoms [139, 140]; are more likely to report mistreatment during childbirth [141]; report that their providers frequently used language or tones that suggest a devaluation of Black reproduction [140]; were less likely to be provided education and encouragement around breast feeding [142]; and providers were less likely to comply with birth plans or solicit consent to initiate cesarean births [143].

The subjective experience of care can often differ from the actual content of care offered, and in an era where there is increasing pressure to serve more patients with fewer resources, many providers are frustrated that they are denied the ability to build deeper relationships with patients. Nevertheless, there is considerable evidence to suggest that some forms of differential practice based on patient race are ongoing throughout American medicine [144, 145]. Black patients are less likely to receive certain cardiac procedures [146], laparoscopic surgical approaches [147], optimal and timely cancer care [148–151], and kidney transplant [152, 153]. The 2018 National Healthcare Quality Report from the Agency for Healthcare Research and Quality found that Blacks, American Indians and Alaska Natives, received worse care for 40% of quality measures and for Hispanics, worse care for 35% of quality measures [154]. Moreover, research shows that the higher the level of unconscious bias in providers, the less likely they are to offer treatment to Black patients. This is reflective of a not-inconsiderable body of research on medical students, trainees, and providers that consistently show a bias towards White patients when considering accuracy of symptom reporting, experience of pain versus drug seeking behavior, trust in care compliance, and willingness to prioritize longer-term, more costly, less invasive treatment plans [134, 155–157]. Female providers show lower levels of bias, although both female and male White providers displayed more bias than Black providers, who test as neutral [158]. Bias and differential treatment has a tangible impact on the health outcomes of patients. While the evidence is mixed for positive health outcomes more generally [159], several studies indicate that gender and race concordant care is associated with increased utilization of healthcare and preventative screening, improved provider-patient communication, and patient compliance with treatment plans [160–165]. Together, this data suggests that the act of seeking medical care may be an additional stressor for women of color, potentially contributing to rather than mitigating negative health outcomes.

Addressing Allostatic Load in Pregnancy Care

There is thus ample evidence that women of color *arrive* at prenatal care at increased risk of pregnancy complications due to factors that are not linked directly to income and education level. These systemic factors must be addressed in concert with efforts to improve technical aspects of medical practice and data collection [166, 167]. Accumulating evidence suggests our approach to remediating racial health disparities must include addressing disproportionate allostatic load as a result of racism and socioeconomic disadvantage.

Social justice frameworks are increasingly recognizing the importance of not only equal access to quality healthcare, but an individual human right to the highest achievable physical and mental health. The magnitude of maternal-fetal health disparities, as well as the pervasive and systemic nature of interpersonal and structural racism, suggests the promotion of healthy behaviors among women of color as a resilience-building strategy is not enough to compensate for the cumulative physiological effects of increased stress prior to pregnancy. As evidence suggests these stressors are largely beyond individual control, but are rather the products of living in a society which places women of color at a significant disadvantage, the remedy must be broader than placing responsibility for improved health behaviors on individuals. This is especially the case since at-risk women may lack the psychosocial and economic means for self-improvement. Instead, collective action is needed to address elevated allostatic load and its underlying causes by individual medical professionals, institutions, and by society and its legislative bodies.

Ideally, such measures would include substantive investment in public health, social programs, and the economic advancement of the most at-risk populations. This additional investment is consistent with principles of distributive justice and is a particularly salient consideration given the under-resourced nature of many minority communities. It also is likely to result in significant societal benefits, including reduction of medical costs and increased productivity and economic contributions through advancing the health of women and their children. Adverse pregnancy outcomes impact the health care system as a whole. Maternal and neonatal complications are resource-intensive and result in significant healthcare costs. Caring for mothers with preeclampsia alone costs \$2.18 billion per year; these costs are disproportionately generated by preterm births [168]. Severe maternal morbidity more than doubles the cost of a delivery hospitalization, raising it from \$4,300 to \$11,000 on average [169]. While only accounting for 8% of infant hospital stays, costs for preterm birth and low birthweight infant admissions account for almost half of all infant hospitalization costs and one quarter of pediatric costs in the US [170]. Stillbirths are also associated with significant hospital costs compared to live births, requiring diagnostic tests, additional treatments for maternal complications, and longer lengths of stay.[171] Furthermore, women may be unable to work for a period of time after experiencing pregnancy-related complications, imposing a financial burden on their family. The true cost of maternal mortality is perhaps incalculable, disrupting the functioning of entire families and communities and carrying the consequent loss of productivity [172]. Moreover, preterm birth is associated with long-term morbidity, placing future generations at increased risk of poor health and its related psychosocial and economic effects. From birth to early childhood

alone, the adverse clinical sequelae associated with preterm birth is estimated to cost the U.S. a minimum of \$26.2 billion annually [173].

Failure to redress disproportionate elevated allostatic load perpetuates historic and present-day injustices towards people of color and continues to prevent equitable health. The evidence indicating that allostatic load may have a significant epigenetic component suggests we are still bearing the costs of slavery and systemic discrimination. The ramifications of these injustices will only continue to perpetuate through generations unless we take intervening action. However, the accretion of decades of social inertia on race and present trends suggests there is unlikely to be sufficient momentum at the legislative level. Thus, we turn to the role of providers and their institutions in addressing racial disparities in pregnancy outcomes, including doing more to recognize and counter the impacts of elevated allostatic load on pregnancy outcomes. This includes proactive attempts to reduce implicit bias and discrimination and the courage to examine and address institutional factors that may contribute to racial- and gender-based stress.

Elevated allostatic load is conceptualized as a chronic, lifelong condition. It is not triggered episodically or even semi-episodically such as via low-quality care during a single pregnancy. Nevertheless, the data are compelling that the physiological results of elevated allostatic load may exacerbate existing pregnancy risks. The psychological and subjective experiences of care during pregnancy may both contribute to allostatic load and provide a disincentive to access and utilize the care necessary to compensate for it. This suggests that pregnancy care providers need to be increasingly conscious of their role in contributing to allostatic load during pregnancy and birth. Based on what is known about the physical impact of race-related stressors such as interpersonal discrimination, biased encounters with care providers may contribute to the long-term effects of allostatic load. One-third of African Americans report that they have been discriminated against when going to a doctor or health clinic, and one-fifth of African Americans have avoided seeking health care due to concerns of discrimination or poor treatment [174]. In the prenatal setting, Black women have reported perceptions that their provider made negative stereotypical assumptions about their status regarding insurance, marriage, and substance abuse, resulting in unfair treatment [140]. These kinds of incidents alienate women from their providers and impede the delivery of high-quality care, which is critical to reducing outcome disparities. Explicitly biased interactions also affect quality of care. Microaggressions by White doctors serve as a source of race-related stress in the clinical setting, harming the patient-physician relationship and discouraging patients from seeking medical help [175]. Bias and discrimination in the healthcare setting violate the principle of non-maleficence, generating feelings of distrust and animosity instead of facilitating healthy outcomes.

A current focus should also be on implementing measures to mitigate the effects of chronic stress before, during, and after pregnancy. Improving access to social resources and fostering community engagement may be among the most effective resilience-building strategies for overcoming stress [71]. Historically, political willingness to invest in low-income, majority-minority neighborhoods has been minimal due to a lack of capital and of the perceived lack of political power in these populations [70]. We are seeing the results. Resources should be devoted to community-based initiatives to improve access to quality healthcare. Such efforts

should be enacted in concert and with continual feedback from the communities they serve, so that they are not only effective, but so women and their families are treated as equal partners in promoting the health and flourishing of their community. Specifically, the use of community health workers, doulas, and/or community-based support groups during pregnancy may help reduce maternal and infant morbidity and mortality [176, 177]. These services would improve patient empowerment, access to healthcare providers, social support, and patient education, providing tools for coping with stress and supporting healthier pregnancies [178]. Pilot studies have demonstrated that doula support for low-income Latina and Black women results in lower rates of preterm birth, low birthweight, and cesarean delivery, as well as increased breastfeeding initiation and duration [179–181]. Doulas can educate patients, address issues of health literacy, and lower women's stress during pregnancy, labor, and delivery [182, 183]. In situations in which patients reported trust in their prenatal provider and believed that they had a meaningful relationship, differences in outcomes and accessing care significantly decreased, suggesting the facilitation of continuous trusted care may lead to greater adherence and compensate for stress accumulation prior to the clinical encounter [184, 185].

Maternal-fetal morbidity and mortality results in significant harms to women, children, communities and society through increasing healthcare costs, decreasing productivity, and threatening autonomy and self-determination. Devoting resources to supporting minority women and working to counter the effects of chronic stress before, during, and after pregnancy could greatly improve birth outcomes, narrowing the racial gap in adverse pregnancy outcomes. Greater understanding of allostatic load and its role in pregnancy outcomes is needed among healthcare providers and other stakeholders, including the effects of implicit and explicit racism on individual health. Furthermore, it is essential to prioritize the investigation of why these disparities persist through improved data collection on maternal and infant morbidity and mortality. This may help resist the easy narrative that patient factors alone are the source for outcome gaps that exist on a outcomes, there are strong moral and material incentives for countering the effects of chronic racial stress.

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