Biologic Measures as Epidemiological Indicators of Risk for the Development of Hypertension in an African American Adolescent Population

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Globally, the health disparity of hypertension is disproportionately greater within the African American population. Epidemiological data describe African Americans as a vulnerable population with a high incidence and a greater risk of developing essential hypertension (HTN).\(^1\) The prevalence of HTN, which develops at an earlier age in African Americans, is 41% compared with the Caucasian population (28%).\(^2\) As a chronic and progressive disease, HTN is the gateway to target organ diseases including blindness, renal failure, ischemic heart disease, and cerebral vascular disease.\(^3\)

Biologic measures, including elevated blood pressure (BP), hormonal stress responses, hyperresponsive sympathetic reactivity (the exaggerated increase of BP and cortisol in response to stress), and known family history of hypertension (FHH), have been correlated with BP changes that precede the subsequent development of EH.\(^4\),\(^5\) It is thought that the continuous existence of hypertension risk factors during childhood and adolescence may be precursors and indicators of risk for BP changes and the subsequent development of adult hypertension.\(^6\),\(^7\)

Within the general community, young adults tend to enjoy general good health and have less participation within the healthcare system. There is a gap in...
the research about young adult populations, especially within the African American population. Studies on the prevalence of biologic risk factors in adolescents and, in particular, African American adolescents are sparse. The epidemiological study within an African American adolescent population of vascular and neuroendocrine risk factors provides a unique perspective of biologic measures as indicators of risk that may contribute to the knowledge of elevated BP development and may contribute to assessment and preventative intervention for hypertension. A previous study of hypertension risk factors of African American adolescents (14–17 years) reported an increased prevalence of FHH, prehypertension, elevated cortisol levels, and hyperresponsive BP (cardiovascular reactivity [CVR]) and cortisol measurements to physiological stress. The previous study had a smaller sample size and was a secondary analysis. The purpose of this study was to further describe the prevalence of biologic measures of risk of hypertension development in African American adolescents and revisit findings within a similar population 4 years after the previous study.

Background

Multiethnic/racial studies reported an ethnic and gender gap in prehypertension whereby African Americans had a greater prevalence of prehypertension (15.9% for males and 9.6% for females) compared with non-Hispanic whites males (12%) and females (5.9%) and a 4.2% prevalence of high BP compared with 3.3% for the non-Hispanic white population. Compared with non-Hispanic white adolescents, African American adolescents also have a higher causal and ambulatory systolic and diastolic BP and greater variability that increases with age.

African American ethnicity has been associated with a variety of physiologic alterations that influence BP regulation in studies of both adolescents and adults. Observations from the Bogalusa Heart Study found that compared with Caucasian American adolescents of European descent, African American adolescents have higher resting BP even without obesity; differences in electrolyte handling of sodium and potassium and BP levels and variability in early life are predictive of adult hypertension.

Blood pressure regulation and the development of hypertension are multifactorial and polygenic processes. Essential hypertension, which constitutes 90% of hypertension cases, is a multifactorial disease combining genetic, physiological, and environmental factors regulating BP. Although the underlying mechanisms are complex and poorly understood, the interaction of polygenic and environmental-behavioral factors may contribute to the pathological alterations that increase BP. The concept that functional and structural alterations in the vasculature, such as vasculature remodeling, decreased compliance, and increased peripheral resistance, may antedate EH and contribute to its pathogenesis has gained clinical support.

Within this study, biologic measures are explored, specifically, elevated BP, cortisol, hyperresponsive BP, and cortisol levels in response to induced physiologic stress and FHH. Arterial BP is determined by the physical factors of arterial blood volume and arterial compliance, which in turn are affected by physiological factors of cardiac output (heart rate × stroke volume) and peripheral resistance. Renal, cardiac, and neuroendocrine hormones influence the regulation and maintenance of BP. A number of alterations, including cardiac, renal, endocrine, and central nervous systems; genetics; environment; and stress, have been implicated in the genesis of EH. Alterations include increased sympathetic nervous system activity caused by increased exposure or response to psychological or physiologic stress; overproduction of salt retaining and vascular constrictor hormones, including cortisol, angiotensin II, and aldosterone; increased renin secretion with increased production of angiotensin II and aldosterone; decreased production of nitric oxide and prostacyclin; alterations in adrenergic receptors that affect heart rate and vascular tone; alterations in renal salt handling; long-term high-salt and low-potassium dietary intake; diabetes mellitus and insulin resistance; and increased vascular growth.

There are identifiable single gene causes of hypertension (eg, Liddle syndrome), but they are uncommon. Research findings suggest that multiple genetic loci have small effects on BP. Genetic mutations affecting BP include renal sodium and water balance, adrenal hormone excess, decrease in nephron number, alterations in rennin-angiotensin-aldosterone hormones, deficiency of nitric oxide, the number of adrenergic receptors, and the increased sympathetic response to stress.

The designation of prehypertension is used to identify individuals at risk for developing EH. Continuous BP elevation has been correlated with future development of EH. Findings described in the Bogalusa Heart Study15,17 that showed childhood BP elevations serve as a good predictor of elevated and hypertensive BP in adulthood.

The exposure to acute or chronic stress stimulates the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis resulting in the release of epinephrine and cortisol. Cortisol affects fluid and electrolyte balance and consequently BP. Blood pressure is increased by the attenuation of sodium excretion and increased vasoconstriction, thereby causing vascular remodeling and hypertrophy. Cortisol levels (serum and salivary) provide a reliable measure of hypothalamic-pituitary-adrenal axis activity, which is generally accepted as a physiological index of stress.
Correlation of elevated cortisol to an increased systolic BP in early adolescence has been described.\textsuperscript{22}

Hyperresponsive BP and cortisol have been associated with the development of vascular calcification, vascular remodeling, ventricular hypertrophy, and hypertension.\textsuperscript{20,23,24} Hyperresponsive BP and cortisol changes due to stress are considered strong physiological indicators of the development of EH.\textsuperscript{25,26} African American adolescents have a larger percentage of peripheral α- and β-adrenergic receptors; demonstrate heightened vasoconstrictive vascular responses to stressors,\textsuperscript{3,24} greater CVR to stress,\textsuperscript{24,26} and lower values of renin in the presence of normal to low levels of aldosterone; and respond more slowly to sodium load\textsuperscript{27} than do Caucasian adolescents.

Studies in adolescents\textsuperscript{28} and young adults\textsuperscript{20} reported elevated BP, and the increase of BP in response to stress may be predictive of daily activity BP elevations and variability and the development of EH. Research\textsuperscript{24} within a general adolescent population demonstrated a prospective relationship between exaggerated or hyperresponsive CVR to stress and an increase in resting BP over a 3-year period and the subsequent development of EH.

Essential hypertension tends to cluster in families and offspring of individuals with EH, who have a greater risk of developing elevated BP.\textsuperscript{29} A positive FHH is a complex risk factor that has biologic significance as a reflection of the interaction of multiple genetic loci that regulate BP.\textsuperscript{3,4} Research results indicate that children with an FHH have elevated sodium loading and increased vascular resistance responses to extended stressors compared with children of normotensive parents and manifest greater systolic and diastolic pressure changes in response to stressors.\textsuperscript{3,4,29} Studies\textsuperscript{18,29} of African American adolescents reported that adolescents with an FHH exhibited higher resting BP and CVR than do Caucasian adolescents with a similar history.

For this study of African American adolescents within a high school population, we examined the following questions:

1. What is the prevalence of biologic measures of risk of hypertension specifically FHH, prehypertension, elevated salivary cortisol, hyperresponsive cortisol, and CVR?
2. Is there gender difference in the prevalence of biologic risk factors of hypertension?

**Methods**

**Study Participants**

To describe the prevalence of biologic measures of risk of EH within an urban African American adolescent high school population (14–18 years), an exploratory descriptive design with a nonrandom purposive sample was used. Participants were recruited from a historically African American high school (9th–12th grades) with student population of 1000, located in an urban, low socioeconomic community in Florida. Participants were drawn from students (N = 150) enrolled in 4 classes of Personal Fitness and Life Management over two 9-week course sections. Within the school curriculum, these courses are generally taken in the 9th and 10th grades with older students participating because of previous schedule conflicts, school transfer, or failing grades. These courses were selected because, as required courses, students were representative of the general student population and not particular academic tracts. Permission to conduct the study was obtained from school principal, course teachers, and university institutional review board.

As a means of introduction to potential participants and ameliorate measurement anxiety, the study investigator presented a “health promotion” lecture to each class. Content included cardiovascular health, BP concepts, measurement, and interpretation. Students received American Heart Association Web site resources and literature concerning African Americans and hypertension risk. All students were given the opportunity to operate the automatic BP measurement device and interpret results. In a subsequent class, the study investigator presented a study overview. It was emphasized that participation was voluntary and would not influence class grading, and the salivary sample would be used solely for cortisol level measurements. A cover letter sent to parents/guardian included name, professional information and contact information of the study investigator, the study description, consent form, participant assent form, and request for health information. The project was described as a nursing study of BP and cortisol levels (a normal chemical produced in the body) in teenagers. Blood pressure measurement, cortisol saliva collection assay, and the technique of placing the hand in cold water for 1 minute to produce stress were described. The letter explained that participation was voluntary, it was not part of the class grade, participants would know their BP measurement findings, and parents/guardians would be notified of BP that required medical follow-up. Parents/guardians were asked to provide health information concerning their child, specifically diabetes and circulatory problems, and indicate if they or a close family member (eg, mother of child, grandmother of child) had a history of EH or high BP. A family member category list was provided with the instruction to encircle the member with EH.

Participants who met the criteria of African American A ethnicity, were 14 to 18 years old, signed parental consent, signed participant assent, and completed the...
demographic form were included. Adolescents with a history of peripheral circulation problems or diabetes were excluded because the study protocol included cold water hand immersion. Participants who completed the study activities/protocol received a $10 honorarium.

One hundred sixteen students (77%) participated, and of these, 106 (92%)—49 males and 57 females—completed the study. For the 34 adolescents who did not participate and/or did not meet inclusion criteria, reasons included class absence and attrition, unsigned parental consent form, and “don’t want to bother.” Ten participants had incomplete data related to class or school attrition, and their data were excluded from analysis.

**Procedures and Measures**

Biologic measurements were conducted by the study investigator during week 1 and week 4 of the study in a quiet area between the hours of 0800 and 1000 to maintain circadian consistency. Height measurements without shoes were obtained. Participants sat quietly for 5 minutes in the designated study area before measurements. Blood pressure measurements were taken in a sitting position on the left arm using an appropriate size cuff and a DINAMAP Compact Monitor Model S automated oscillometric BP device (Critikon 1998, Tampa, Florida). This digital output automated device determines systolic and diastolic BP and maintains reliability across assessment times. The Critikon manual indicates a systolic and diastolic reliability of $P < .05$, with a drift factor of 3 mm Hg systolic and 2 mm Hg diastolic that is more prominent at elevated physiologic stress.

The recorded BP categorization was based on the average of 2 properly measured BP readings measured at a 3-minute interval. Blood pressure was classified as (1) normal at the 90th percentile or below and below 120/80, (2) prehypertensive between the 90th and 95th percentiles, or (3) hypertensive at the 95th percentile or above according to gender, age, and height criteria of the Task Force on High Blood Pressure in Children and Adolescents. This also optimized the reliability of BP classifications. As BP classification is based on auscultation and the BP readings for this study were obtained via an automated oscillometric BP device, categories for BP were assigned based on extrapolation from the guidelines for auscultation.

Salivary cortisol is a simple, noninvasive, relatively stress-free measure of response to a stressor and is comparable to serum cortisol measures. Cortisol levels vary in circadian fashion with the highest level in the morning and lowest at night; therefore, all specimens were collected in the morning between 8 and 10 AM. Normal values for 13- to 17-year-olds are within adult ranges and percentiles. Published reports indicate a normal morning value of 10 to 18 nmol/L. Correlations of saliva and serum cortisol measures range from 0.83 to 0.93 nmol/L. For this study, a morning salivary cortisol level of 18 nmol/L or above was categorized as elevated.

On the day before testing, participants were instructed not to eat a major meal within 60 minutes before sample collection. Saliva was collected by using a cotton swab and saliva-collecting tube (Salivette, Salimetrics, LLC, State College, Pennsylvania). Participants were instructed to place a cotton swab in the mouth for 2 minutes timed by the research assistant to allow for sufficient saliva volume absorption and then place the swab into the provided collecting tube. Saliva specimens were frozen and stored at $-20^\circ$C for future assay.

Cortisol was measured by radioimmunoassay using a polyclonal rabbit anticortisol antiseraum. Before assay, 10 $\mu$L aliquots of saliva samples were deproteinized using 1 mL of ethanol. This assay method has been previously described. Assays were performed by the investigator in a controlled laboratory setting to ensure quality control. Sensitivity of this assay was 10 pg/sample. Control samples run in each assay had interassay and intraassay coefficients of variation less than 12% and 10%, respectively.

Blood pressure and cortisol reactivity were determined by the difference between resting (basal) and the peak BP and cortisol levels induced by physiologic stress. For this study, hyperresponsivity to induced physiologic stress was defined as a 20 mm Hg increase of systolic and/or diastolic BP above the resting BP and a cortisol response one and a half times the peak BP and cortisol levels induced by physiologic stress.

The cold pressor test of hand immersion to induce physiologic stress was used to determine reactivity. A 12 in $\times$ 9 in $\times$ 12 in plastic container was filled with cold water at 4°C to 5°C (39–41°F). Temperature was measured with a standard waterproof pool temperature gauge that had both Celsius and Fahrenheit indicators. Stress was induced by placing the right hand up to the wrist in cold water for 50 to 60 seconds as tolerated. Time was measured to the nearest second with an automatic timer. This methodology has been used in many research studies and has been reliable for inducing physiologic stress reactions, and stability of vascular and myocardial response patterns has shown that the test is reliable.

Blood pressure measurements and salivary samples were obtained immediately before the cold pressor test for each participant as a baseline measure. A second BP was measured immediately upon hand removal from the water. Cortisol levels peak 20 to 30 minutes...
after a stressor and return to normal range within 60 minutes; therefore, the second salivary sample was collected 20 to 25 minutes after hand removal from the water.

**Data Analysis**

Descriptive statistics were used to obtain the summary results for analysis. Two-sample t test and analysis of frequency ($\chi^2$) were used to test for gender differences in FHH, BP, cortisol, and sympathetic hyperresponsivity. All analyses were completed using SAS 9.1 (SAS Institute Inc, SAS Online Doc 9.1.3, Cary, North Carolina, 2002–2005). Statistical significance was evaluated at $P < .05$ for all analyses.

**Results**

One hundred six African American participants (49 males and 57 females) completed the study. Table 1 describes the frequency and percentage of participant demographic data and individual biologic measures of risk. Seventy-five of the 106 participants (71%) reported a positive FHH. There was no gender difference in the prevalence of FHH ($\chi^2 = 2.59$, $P = .19$). A grandmother was the most common family member identified (79%), followed by father (25%) and mother (20%).

The mean (SD) overall resting BP of the total group (N = 106) was 120 (14) mm Hg systolic and 68 (7.7) mm Hg diastolic. Systolic BP was higher in men compared with women ($t = 2.72$, $P = .001$). In contrast, men and women had comparable diastolic BP. Forty-three (41%) participants had elevated BP. Elevated BP was more prevalent in men than women ($\chi^2 = 8.0$, $P = .005$). The mean (SD) BP for the elevated BP group (n = 43) was 132 (13) mm Hg systolic and 72 (3) mm Hg diastolic.

Ninety-one participants (86%) had salivary cortisol levels above 18 nmol/L. The group mean (SD) resting cortisol level was 26 (11.5) nmol/L. There was no difference in cortisol levels by gender.

Fifty-two participants (49%) had hyperresponsive systolic and/or diastolic CVR. The mean (SD) BP reactivity ranges were 16.5 (12) mm Hg systolic and 10 (4.2) mm Hg diastolic pressure. There was no statistical gender difference. Thirty-seven participants (35%) had hyperresponsive cortisol levels. Blood pressure and cortisol reactivity were comparable between men and women.

In addition to being African American, the number and percentage of participants with multiple biologic measures of risk of FHH, prehypertension, hyperresponsive CVR, elevated cortisol, and hyperresponsive cortisol are presented in Table 2.

**Discussion**

Blood pressure regulation and the development of EH are multifactorial processes. Elevated and continuous interaction of biologic measures (African American ethnicity/race, prehypertension, cortisol and hyperresponsive BP, cortisol levels, and FHH) contributes to the risk of developing hypertension. The prevalence of individual biologic measures as indicators of risk for the development of hypertension and the number of participants with 3 or more measures within this study of African American adolescent (mean age of 15 years) population add support to the designation of African Americans as vulnerable population at high risk of developing EH.

The overall group BP means were higher for both genders compared to findings from an epidemiologic study of mixed ethnicity adolescents that reported a mean systolic BP of 106 mm Hg and diastolic BP of 61.7 mm Hg, with values for African American females 1.6 mm Hg higher and for African American males 2.9 mm Hg higher for systolic and diastolic pressures. In this study, both males and females had higher systolic pressures than expected but these were consistent with our previous study. The number of males with elevated systolic BP and the number of participants with prehypertensive BP are clinically significant at this young age. A study of Dutch adolescents described the increase of risk of EH, 8% in girls and 3% in boys, for every 1 mm Hg above 120 mm Hg systolic BP. The study may be limited in its ability to generalize to an African American adolescent population, but it does provide support for the high risk of EH development. Longitudinal studies of African American adolescents would elucidate the development of EH in later decades.
Two male participants had hypertensive BP; one was under the care of a physician and the other’s parents were notified by the study investigator and provided BP measurements for follow-up with their healthcare provider or local health clinic. Participants with prehypertensive BP were provided copies of their pressures and provided with American Heart Association resources.

The increase in BP may be attributed to a number of interrelated factors, including chronic stress, diet, sodium intake, salt sensitivity, physical inactivity, smoking, alcohol intake, drugs, and body mass index. A common anecdotal theme within this group, gleaned by the study investigator in casual conversations with participants, was the food preference for high-sodium foods including pepperoni pizza, french fries with extra salt, and the popularity of a local “fast food” restaurant. An increased prevalence of salt sensitivity is attributed to individuals of African American ethnicity. Although the cause of salt sensitivity is poorly understood, there is a direct correlation of dietary salt intake and BP.13 Expanded extracellular volume, disturbances of the renin-angiotensin-aldosterone system, and altered sodium conservation are all related to BP changes that may lead to EH.4

The elevated cortisol mean and the high number of adolescents with elevated cortisol describe a group at risk for development of elevated BP. Persistent and chronic elevations of cortisol affect sodium and fluid retention and, over a prolonged period, would subsequently increase BP.4 Although research correlating elevated cortisol levels and adolescent EH, especially in African Americans, is sparse, higher than normal cortisol levels have been reported in adults with EH.25

Elevated levels of cortisol indicate stress and may have both physiological and sociopsychological contributors.19 Research findings40,41 reported elevated morning cortisol levels of African American adolescent males in a low socioeconomic status (SES) community. The inclusion of afternoon and evening cortisol measurements in future research would expand the knowledge of the circadian influence. The addition of cortisol studies related to ethnicity, gender, age, and interrelated psychological and physiological stress measurements within diverse SES adolescent groups would further elucidate the neuroendocrine responses to stressors.

Stress hyperresponsivity is meaningful as a predictor of EH when examined in combination with genetic susceptibility.30,31 Adolescents with hyperresponsive CVR have a 5 times greater risk of developing EH than those with a lesser response.42,43 In light of the elevated BP and cortisol measurements for this African American adolescent group, the percentages of participants with hyperresponsive CVR and hyperresponsive cortisol levels are clinically noteworthy. The response to stressors begins at a higher level and extends to an elevated level thereby compounding the influence of pressure and hormonal interactions. Studies44,45 have demonstrated that these factors add stress to vascular walls and cause left ventricular hypertrophy and vascular calcification, which in turn cause higher sustained pressure and hypertension.

The elevated overall group resting cortisol levels and number of participants with hyperresponsive BP and cortisol response to stress support the findings46,47,48 for the link of SES, CVR, cardiovascular disease and hypertension in African American populations. The measures may be related to the greater number of stress-related problems and disparity in access to healthcare in low SES groups.41 The addition of SES and healthcare disparity factors in future research would add to the knowledge of EH in the adolescent population.

Although a positive FHH is not an exact measurement, it provides insight of a genetic biologic indicator of risk for EH development. The prevalence of known FHH (71%) is higher than the reported 40% for adult African Americans,46 and the results were similar to our previous study. The difference may be related to differential self-reporting between adolescents and adults. The broad classification of a positive FHH designated by a parent, sibling, and/or grandparent with hypertension, within this population, may have also influenced the number reporting an FHH.

Environmental factors of SES (eg, nutrition, exercise, economic stress, healthcare access, and racial prejudice) cannot be overlooked as they interact with the physiological systems and contribute to overall health.47,48 Although participant SES was not obtained, the high school serves an urban, low socioeconomic community. Research studies of African Americans with more diversified SES groups and verified family history and environmental data are needed.
Limitations of the Study

Limitations of this study include the small number of adolescent participants, the lack of ability to validate self-reported data, and lack of long-term follow-up. The FHH was dependent on reported data, which have the inherent problem of questionable accuracy. Although the orientation to the study investigator and measurement tools was provided, the “white coat effect” of anxiety cannot have been eliminated for BP and cortisol measurements. Although studies by Chen et al. indicated that elevated BPs were independent of obesity, the addition of body mass index and waist circumference would have added to the study. Participants were very reluctant to have weights measured probably because of the classroom atmosphere. Longitudinal studies that correlate physiological risk factors with BP changes would add to the knowledge of EH development. The elevated level of cortisol found in this sample may be attributed to a methodological or laboratory assay factors; however, measurements were conducted using standard procedures and reliability controls.

The number of participants and the selected setting limit the generalization of the findings but do add a distinct perspective on the prevalence of biologic measures of risk in a specific population susceptible to hypertension.

Implications for Nursing Practice

The findings of this study propose evidence that routine BP assessments in adolescent populations are essential and elevated BP levels in stressful situations should not be dismissed as inconsequential. Environmental stress may be reflected in elevated BP measurements and cortisol levels. The hyperresponsive CVR may be indicative of the variability of BP levels that occur with daily stress. The high prevalence of multiple risk factors illustrates the need for health promotion education. Genetic and biologic measures of risk factors may not be modifiable, but they provide a rationale for the biologic mechanism of action, implementation, and emphasis on positive lifestyle behaviors such as diet, exercise, no smoking, and stress reduction.

Conclusion

The prevalence of biologic measures of risk for hypertension adds to the knowledge of BP regulation and risk of development of hypertension in an urban African American adolescent population. The findings of this study are consistent with the previous study. Study participants were young and healthy. Besides of the higher than expected BP and the increased prevalence of individual risk factors, the number of participants with multiple biologic measures of risk as described in Table 2 is clinically noteworthy. The continuous interaction of biologic measures over time may increase the susceptibility and risk of EH development. The prevalence of these measures supports the hypothesis that EH originates in adolescence and that the continuous existence of the risk factors may be the precursors to the development of EH in adulthood. The addition of environmental and behavioral factors including obesity, inactivity, stress, diet, smoking, and so forth may further compound and enhance the risk for the development of EH.

A primary goal of Health People 2020 is to decrease the incidence of hypertension. Identifying biologic measures of risk within a group provides a primary and relevant focus for community and school health promotion assessments, interventions, and initiatives. Health promotion interventions that focus on cultural-ethnic-biologic-behavioral factors would enhance healthcare knowledge and practices.

REFERENCES


