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Jonathan D. Mosley, Lawrence J. Appel, Zeinab Ashour, Josef Coresh, Paul K. Whelton and M. Mohsen Ibrahim

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# Relationship Between Skin Color and Blood Pressure in Egyptian Adults

## Results From the National Hypertension Project

Jonathan D. Mosley, Lawrence J. Appel, Zeinab Ashour, Josef Coresh,  
Paul K. Whelton, M. Mohsen Ibrahim

**Abstract**—In many, but not all societies, dark skin color is associated with high blood pressure. Whether the association between skin color and blood pressure is independent of known determinants of blood pressure remains controversial. We examined the association between skin color and blood pressure in 835 Egyptian adults (370 men and 465 women) participating in the National Hypertension Project, a national survey of hypertension prevalence and blood pressure–related complications conducted in Egypt during 1991–1993. Skin color was assessed by measuring the concentration of cutaneous melanin in an unexposed area with the use of reflectance spectrophotometry. Higher concentrations of melanin were associated with lower body mass index, less education, manual labor (among men), and a lower urinary sodium-to-potassium ratio (among women). In multivariate regression analyses adjusted for age, body mass index, and education, there was a significant nonlinear association between blood pressure and skin color among women; in the lower to intermediate range of skin pigmentation, both systolic and diastolic blood pressures were higher in women with greater concentrations of cutaneous melanin. In men, blood pressure was not associated with skin color. When we used a subjective assessment of skin color, there was no significant difference in blood pressure between black-skinned Egyptians (predominantly of Nubian descent) and fair-skinned Egyptians for either gender. While the significant relationship in women appeared to be independent of known risk factors for hypertension, residual confounding may explain the association. (*Hypertension*. 2000;36:296-302.)

**Key Words:** skin color ■ spectrophotometry ■ blood pressure ■ race

A high prevalence of hypertension among black Americans, compared with their white counterparts, has been a persistent observation in the United States.<sup>1</sup> A similar pattern has also been identified among blacks living in Europe, South America, and other interracial societies.<sup>2</sup> However, with the exception of South Africa, low rates of hypertension are generally observed among blacks living in Africa.<sup>3</sup>

One explanation for the association of skin color and blood pressure (BP) is an imbalance in the distribution of factors that affect BP. Epidemiological studies have identified a number of variables associated with BP levels, including age, gender, body mass index (BMI), sodium intake, potassium intake, socioeconomic status, alcohol consumption, and physical activity.<sup>4,5</sup> Whether these factors account for the increased rates of hypertension in blacks remains controversial.

A common gene that determines both skin color and BP is another explanation. The genetic mechanisms controlling melanin biosynthesis are complex and poorly understood. In

the mouse, >50 distinct loci have been identified.<sup>6</sup> Kwon<sup>7</sup> has proposed that these genes be divided into 2 families: the tyrosinase family and the pmel 17 gene family. Human genes belonging to this first family include *GP75* (location: 9p23), *TYRP2* (location: 13q31-q32), and *TYR* (location: 11q14-q21). The primary gene belonging to the pmel 17 family is located at 12q13-q14. Genes regulating melanocyte-stimulating hormone and its cellular receptor are located at 2p25 and 16q24.3, respectively.

Still, a genetic link between melanin biosynthesis and BP regulation has yet to be identified. Association and linkage studies have identified several candidate genes for elevated BP: *AGT* (location: 1q42-q43), *ACE* (location: 17q23), *REN* (location: 1q32), and *SAH* (location: 16p13.11).<sup>8</sup> Hence, at least for the present, the genes that might regulate BP do not appear to be linked to those regulating melanin biosynthesis.

A third mechanism explaining an association between skin color and BP is a common biochemical intermediate. Empirical data suggest that a common biochemical intermediate is

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**TABLE 1. Characteristics of Study Participants by Gender**

Characteristic	Men (n=370)	Women (n=465)
Age, y	50.8 (13.5)	47.2 (12.7)
Governate, n (%)		
Sharkia	117 (31.6%)	133 (28.6%)
Aswan	148 (40.0%)	225 (48.4%)
El Wadi El Gedid	105 (28.4%)	107 (23.0%)
Dwelling, n (%)		
Urban	232 (62.7%)	259 (55.7%)
Rural	138 (37.3%)	206 (44.3%)
Education, n (%)		
None	114 (30.8%)	334 (71.8%)
Primary	130 (35.1%)	79 (17.0%)
Secondary or higher	126 (34.1%)	52 (11.2%)
Manual labor, n (%)	147 (39.7%)	17 (3.7%)
Smokers, n (%)	137 (37.0%)	2 (0.4%)
SBP, mm Hg	134.5 (20.9)	134.6 (23.6)
DBP, mm Hg	83.5 (11.7)	80.1 (11.8)
Melanin Index	111.2 (47.2)	85.4 (35.4)
Subjective skin color, n (%)		
Fair	321 (86.8%)	393 (84.5%)
Black	49 (13.2%)	72 (15.5%)
BMI, kg/m <sup>2</sup>	26.4 (5.5)	28.3 (6.2)
K <sup>+</sup> , mmol/L*	27.0 (17.0, 46.0)	26.0 (17.0, 40.0)
Na <sup>+</sup> , mmol/L*	82.0 (50.0, 124.0)	72.0 (46.0, 108.0)
Na <sup>+</sup> /K <sup>+</sup> ratio*	2.9 (2.0, 3.9)	2.5 (1.8, 3.7)

Continuous data are presented as mean (SD) except for urinary electrolyte excretion, which is presented as median (interquartile range).

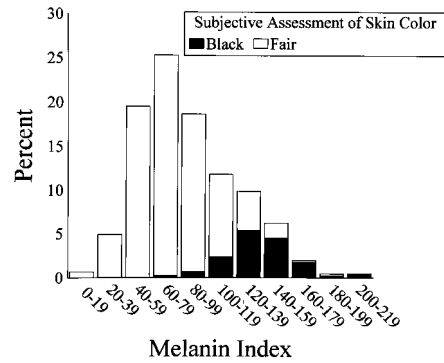
\*12-hour overnight urinary excretion.

plausible. For instance, Lerner et al<sup>9</sup> found that administration of melanocyte-stimulating hormone to study participants resulted in increased pigmentation and, in some cases, increased diastolic blood pressure (DBP) and systolic blood pressure (SBP) levels. In addition, *AGTI*, a gene for a melanocyte-stimulating hormone antagonist located at 20q11.2, is related to skin pigmentation, as well as a predisposition to obesity, cardiovascular disease, and diabetes.<sup>10</sup>

In this setting, we hypothesized that BP rises with increasing levels of skin pigmentation and that this relationship is independent of other known risk factors for hypertension. To test this hypothesis, we used data from the Egyptian National Hypertension Project (NHP). In primary analyses, we used an objective measure of skin color, the Melanin Index, which is a continuous variable derived from reflectance spectrophotometry. In secondary analyses, we used a subjective measure of skin color in which participants were classified as black if they appeared to be Nubian in origin.

**Methods**

The study population consisted of 835 men and women who were participants in the NHP, a study that assessed the prevalence of hypertension and BP-related complications in Egyptian adults.<sup>11</sup> The NHP was a multistage probability survey of household clusters in 6 governates of Egypt. Details of the sampling protocol have been



**Figure 1.** Frequency distribution of Melanin Index in Egyptian women (n=465). Frequency bars are stratified by levels of subjective skin color.

described elsewhere.<sup>11</sup> The study was conducted in 2 phases. Phase I was a hypertension prevalence survey based in 6 governates. Individuals with a mean SBP ≥140 mm Hg, a mean DBP ≥90 mm Hg, or use of antihypertensive drug therapies were defined as hypertensive. Phase II was a follow-up examination of 2313 individuals, ie, 1559 hypertensives identified in phase I and a random sample of their normotensive counterparts (1 normotensive per 2 hypertensives, group-matched on gender and enumeration area). The phase II visit occurred approximately 1 week after the phase I visit. The study was approved by the institutional review board of the Egyptian Ministry of Health. Consent was obtained from all participants.

In phase II, skin color measurements were obtained with the use of a portable spectrophotometer on all but 8 of the 1102 individuals living in Sharkia, Aswan, and El Wadi El Gedid. El Wadi El Gedid represented an exclusively urban-dwelling population, while approximately half of the participants in the other 2 governates were rural dwellers. From this group, 15 were excluded because of biologically implausible spectrophotometric data, 50 as a result of missing data related to the covariates of interest, 6 who were subjectively classified as having “white” skin because they were such a small number, and 188 because they were being treated with antihypertensive medications. After these exclusions, 835 persons (370 men and 465 women) were available for analysis.

**Blood Pressure**

BP was recorded according to a standard protocol adapted from the American Heart Association’s recommended procedures<sup>12</sup> by trained observers using a mercury sphygmomanometer. Four measurements were obtained in phase I of the study, and 2 additional readings were obtained in phase II of the study. The measurements were taken at 5-minute intervals while participants rested quietly in the seated position. In our analyses, the primary outcome variables were SBP and DBP, calculated as an unweighted average of the mean phase I and mean phase II readings.

**Skin Color Measures**

For each participant, a spectrophotometric analysis of skin color was performed with the use of a Minolta spectrophotometer CM-2002. Measurements were taken from the mid-inner aspect of the upper arm, an area unexposed to sunlight. For each individual, the percentage of back-reflected light over the entire visible spectrum (wavelengths between 400 and 700 nm) in 10-nm increments was determined. Reflectance values ranged from 0 (none) to 1 (complete) at each wavelength.

A Melanin Index, derived from the reflectance spectrum, was used as the primary measure of skin color. Derivation of this index was based on principles and methods as described by Dawson et al<sup>13</sup> and Kollias and Baqer.<sup>14</sup> In brief, it has been proposed that taking the log of the inverse reflectance at each wavelength transforms the remittance spectrum into a close approximation of the absorption spectrum. For light with wavelengths between 620 and 700 nm, log of the

**TABLE 2. Bivariate Relationships Between Melanin Index and Hypertension Risk Factors by Gender: Pearson Correlation Coefficients of Melanin Index With Age, BMI, and Sodium-to-Potassium Ratio, and Mean Melanin Index by Level of Education and Occupation**

Risk Factor	Men (n=370)		Women (n=465)	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Age	0.07	0.16	0.11	0.02
BMI	-0.36	<0.0001	-0.36	<0.0001
Na <sup>+</sup> /K <sup>+</sup>	0.002	0.97	-0.11	0.01
Factor	Melanin Index	<i>P</i> *	Melanin Index	<i>P</i> *
Education				
None	135.5 (4.0)	<0.001	91.1 (1.9)	<0.001
Primary	113.5 (3.8)		79.1 (3.8)	
Secondary or higher	81.4 (3.8)		58.1 (4.7)	
Occupation				
Manual labor	127.6 (3.0)	<0.001	n/a†	
Other	100.3 (3.7)		n/a†	

Melanin Index values are mean (SE).

\**P* values for education are for an age-adjusted linear trend test across educational strata. *P* values for occupation are for the age-adjusted difference in mean Melanin Index levels for manual laborers vs other occupations.

†Results not shown because of small numbers within occupational strata.

inverse reflectance values decrease in an approximately linear fashion with a slope proportional to the concentration of melanin in the skin. This slope is defined as the Melanin Index, a unitless, continuous variable objectively quantifying skin color. To facilitate its use, values were multiplied by ( $-1 \times 10^5$ ). In this study, large values of this index are indicative of dark skin.

A subjective measure of skin color was also recorded. Individuals were classified, on the basis of visual inspection by a study interviewer, as either "white," "fair," or "black." The classification took into account both the color of the skin and the racial origin of study participants. The black participants were composed of dark-skinned Egyptians, predominantly Nubians living in the Aswan governate.

### Other Covariates

Basic demographic, socioeconomic, and health behavior information was obtained from a questionnaire administered by a trained interviewer. From a 12-hour overnight urine collection, sodium and potassium excretions were determined, and the sodium-to-potassium ratio was calculated. Subjects were classified as smokers if they gave a positive response to the question "Do you currently smoke?" Weight was measured with a double-beam scale placed on a firm surface, and height was measured with a Frankfort plane positioned at a 90-degree angle against a wall-mounted metal tape. BMI was calculated as weight divided by height squared ( $\text{kg}/\text{m}^2$ ).

Three categories of education were none, primary (through primary school), and secondary (through or beyond secondary school). Occupation was classified as manual labor and nonmanual labor. Most manual laborers were farmers.

### Statistical Methods

In multiple linear regression analyses, SBP and DBP were the outcome variables. Multivariate model building approaches included backward elimination and maximum  $r^2$  methods using all variables that showed a statistically significant association with BP, after adjustment for age. Regression model diagnostics included examining the residuals for normality, inspecting partial regression plots, and examining the change in magnitude of the  $r^2$  terms. All continuous variables were standardized to have a mean of 0 and an

SD of 1. Thus, the  $\beta$  coefficients represented the change in BP per SD increase in these variables. All regression models included age, entered as a series of "dummy" variables representing 10-year age groups. Regression analyses were performed separately for men and women because of a previously reported interaction between gender and age on SBP.<sup>15</sup>

### Results

Table 1 displays characteristics of the 835 study participants, by gender. The mean age of the 370 men was 50.8 years. Almost 70% of the men had some formal education. There was considerable regional variation in levels of education: 41.9% of Aswan men had no education, compared with 28.2% and 18.1% in Sharkia and El Wadi El Gedid, respectively. Forty-nine men (13.2%) were subjectively classified as black, and all but 5 came from Aswan. Approximately 40% of the men were manual laborers; the percentages, by governate, were 51.4% for Aswan, 35.0% for Sharkia, and 28.6% for El Wadi El Gedid. Mean SBP and DBP for men were 134.5 and 83.5 mm Hg, respectively. Their BMI was  $26.4 \text{ kg}/\text{m}^2$ .

The mean age of the 465 women was 47.2 years. Almost half of the women (48.4%) came from Aswan. Women, compared with men, tended to have lower levels of education; 71.8% had no education, and only 11.2% had a secondary level of education. Educational levels were lowest in Aswan (79.6% with no education) and highest in El Wadi El Gedid (50.5% with no education). In general, women did not participate in the work force. Only 3.7% of women performed manual labor. The mean DBP and SBP for women were 134.6 and 80.1 mm Hg, respectively, and their mean BMI was  $28.3 \text{ kg}/\text{m}^2$ . All but 1 of the 72 black women came from Aswan.

**TABLE 3. Age-Adjusted Bivariate Relationships of BP With Skin Color (Melanin Index and Subjective Classification), BMI, Sodium-to-Potassium Ratio, and Socioeconomic Indicators, by Gender**

Independent Variable	SBP			DBP		
	$\beta^*$	<i>P</i>	<i>r</i> <sup>2</sup>	$\beta^*$	<i>P</i>	<i>r</i> <sup>2</sup>
<b>Men (n=370)</b>						
Melanin Index	-0.3†	0.78	0.13	-1.3†	0.03	0.04
Black skin (yes/no)	3.1‡	0.32	0.14	-1.9‡	0.31	0.03
BMI	3.0†	0.003	0.15	2.5†	<0.0001	0.08
Na <sup>+</sup> /K <sup>+</sup> ratio	1.7†	0.11	0.14	1.2†	0.06	0.04
Education						
Primary (yes/no)	4.4§	0.09	0.15	2.2§	0.16	0.05
Secondary or higher (yes/no)	6.4§	0.02		4.4§	0.01	
Manual labor (yes/no)	-3.8¶	0.07	0.14	-2.8¶	0.02	0.04
<b>Women (n=465)</b>						
Melanin Index	3.1†	0.004	0.27	1.5†	0.01	0.07
(Melanin Index) <sup>2</sup>	-1.9†	0.01		-0.8†	0.06	
Black skin (yes/no)	2.3‡	0.40	0.25	1.9‡	0.21	0.06
BMI	1.7†	0.07	0.26	0.9†	0.11	0.06
Na <sup>+</sup> /K <sup>+</sup> ratio	0.8†	0.42	0.25	-0.04†	0.94	0.06
Education						
Primary (yes/no)	1.3§	0.61	0.26	1.6§	0.28	0.08
Secondary or higher (yes/no)	-7.9§	0.02		-5.1§	0.006	

\*Age-adjusted linear regression coefficient, each from separate models.  
 †Difference in BP (mm Hg) per SD increase in the independent variable.  
 ‡Difference in BP (mm Hg) compared with individuals with fair skin.  
 §Difference in BP (mm Hg) compared with the group with no education.  
 ¶Difference in BP (mm Hg) compared with all other occupational classifications.

Figure 1 displays the distribution of Melanin Index for women. The distributions for both women and men are approximately gaussian with a right tail. The average Melanin Index value was 85.4 (range, 12.0 to 212.0) for women and 111.2 (range, 3.2 to 261.0) for men. Among those identified as being black-skinned and fair-skinned individuals, there was considerable overlap in Melanin Index values, primarily in the upper range.

The users of antihypertensive medications excluded from the analyses differed from the study population in several respects. For both genders, those taking antihypertensive medications were more educated (*P*<0.05 for men and women) and had higher BMI values (*P*<0.001 for both) than the study participants. Fewer men taking antihypertensive medications were manual laborers (*P*<0.01), and fewer women taking medications were black (*P*<0.001). Among women, the majority of those taking antihypertensive medications were from El Wadi El Gedid, and the lowest proportion were from Aswan. Among men, the medication users overrepresented Sharkia and underrepresented Aswan, compared with the study participants. Finally, medication users had significantly lower Melanin Index values than the study participants. Male medication users had an average Melanin Index of 87.7 (*P*<0.0001), and female medication users had an average Melanin Index of 68.5 (*P*<0.0001).

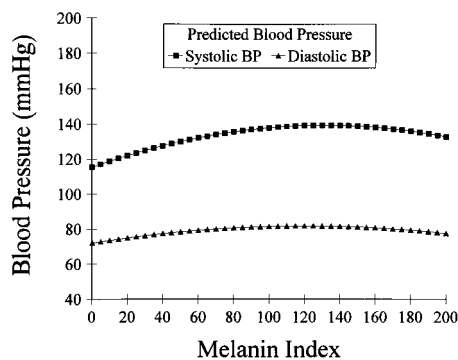
Table 2 displays gender-specific bivariate relationships of Melanin Index to factors commonly associated with BP (age, BMI, sodium-to-potassium ratio, education, and occupation).

Among men, the Melanin Index was inversely associated with BMI (*r*=-0.36, *P*<0.0001), education (*P*<0.001), and occupations other than manual labor (*P*<0.001). For women, the Melanin Index was positively correlated with age (*P*=0.02) and inversely correlated with BMI (*P*<0.0001) and sodium-to-potassium ratio (*P*=0.01). In men, manual laborers had darker skin than other occupational groups (*P*<0.001). Mean Melanin Index levels decreased across increasing educational strata for men and women (*P*<0.001).

Higher levels of education were associated with younger age (*P*<0.001 for men and women), higher BMI (*P*<0.001 for men and women), lower Melanin Index values (*P*<0.001 for men and women), urban dwelling (*P*<0.001 for men and women), fair skin (*P*<0.001 for men; *P*<0.01 for women), and, for men, performing nonmanual labor (*P*<0.001).

Table 3 displays for men and women results from age-adjusted regression analyses in which BP was modeled as a function of 6 factors, each analyzed separately. In men, higher BMI (*P*=0.003) and secondary education (*P*=0.02) were significantly associated with higher levels of SBP. Manual laborers tended to have lower BP than other types of workers (*P*=0.07 for SBP and *P*=0.02 for DBP). Elevated DBP was significantly associated with higher BMI levels (*P*<0.0001) and secondary education (*P*=0.01). Higher levels of the Melanin Index were associated with lower DBP (*P*=0.03).

In women, the relationship between Melanin Index and BP was nonlinear (Figure 2 and Table 3). Specifically, the largest



**Figure 2.** Predicted BP by Melanin Index from least-squared quadratic regression models of SBP and DBP in women (n=465) participating in the NHP of Egypt.

increases in BP per unit increase in the Melanin Index occurred in the low to mid ranges of the Melanin Index; the relationship was attenuated in the upper ranges, where there were fewer observations. Because of the nonlinear association between the Melanin Index and BP, a squared term was added to the Melanin Index model for women. In contrast to men, completion of a secondary level of education was associated with lower levels of SBP ( $P=0.02$ ) and DBP ( $P=0.006$ ).

Table 4 shows the results of multivariate linear regression analyses of SBP and DBP, separately for men and women. Factors considered for inclusion in this model were the covariates listed in Table 3. For men, age and the Melanin Index were forced into the models. Neither SBP nor DBP was significantly associated with Melanin Index in these models.

For women, age was forced into both regression models. A significant nonlinear association between SBP and the Melanin Index persisted after adjustment for BMI and education. A similar pattern was seen with DBP, although the regression coefficient for the squared term was of borderline significance ( $P=0.09$ ). When education was removed from the

**TABLE 4. Multivariate Analyses of Association Between Melanin Index and BP, Adjusted for Age and Other Covariates, by Gender**

Covariates	SBP		DBP	
	$\beta^*$	$P$	$\beta^*$	$P$
<b>Men (n=370)</b>				
Melanin Index	0.9	0.40	-0.5	0.45
BMI	3.4	0.002	2.4	0.002
Na <sup>+</sup> /K <sup>+</sup>	1.7	0.09	1.2	0.04
Model $r^2$	0.16		0.09	
<b>Women (n=465)</b>				
Melanin Index	3.7	0.002	1.7	0.01
(Melanin Index) <sup>2</sup>	-1.8	0.02	-0.7	0.09
BMI	3.2	0.002	1.7	0.004
Education, secondary or higher vs other	-7.5	0.02	-5.2	0.005
Model $r^2$	0.29		0.10	

\*Difference in BP (mm Hg) per SD increase in the independent variable, except for education.

model, the regression coefficients for the Melanin Index and the Melanin Index squared terms in the DBP model were 2.1 ( $P=0.001$ ) and  $-0.8$  ( $P=0.05$ ), respectively. When the multivariate analyses were stratified by governorate, a significant (nonlinear) association between the Melanin Index and BP was observed only in Sharkia. We did not observe any interactions between educational level, skin color, and BP.

In separate analyses, we explored associations between BP and the subjective assessment of skin color (black [predominantly Nubian] versus fair). In these multivariate regression models, the analyses were restricted to residents of the Aswan governorate because virtually all blacks in this study resided in this governorate. The subjective skin color measure variable (classified as Nubian versus non-Nubian) was forced into all models. For both men and women, there was no significant difference between either SBP or DBP between Nubians and non-Nubians.

## Discussion

Consistent with our a priori hypothesis that BP would increase continuously across a gradient of increasing skin darkness, we documented a nonlinear relationship between skin pigmentation, measured by reflectance spectrophotometry, and BP in women. This relationship persisted in multivariate analyses that included age and BMI as covariates. Specifically, in the low to intermediate range of skin pigmentation, both SBP and DBP rose with increasing skin darkness. In the higher ranges, however, the relationship was flat. In the highest range, where there were few observations, BP may have decreased to a small extent. No significant association between the Melanin Index and BP was observed in men. For both genders, Nubians had BP similar to their non-Nubian counterparts. The latter finding provides strong evidence that elevated BP does not inevitably occur in a dark-skinned population residing in a multiethnic society.

A major strength of this study was the use of an objective skin color measure that was proportional to the concentration of cutaneous melanins. Previous studies using spectrophotometric data measured skin color at specific wavelengths within the visible spectrum. In contrast, the Melanin Index used in this study measured skin color in the ranges where melanins are the primary light-absorbing compounds. Another strength was the availability of a large, well-characterized study population with a wide distribution of BP and skin color. Potential limitations include the cross-sectional design of the study and the lack of data on certain covariates (eg, measures of diet other than sodium and potassium and satisfactory measures of physical activity).

Five previous studies have examined the relationship between skin color and BP using a continuous measure of skin color derived from reflectance spectrophotometric data. The findings across these studies have been inconsistent. Boyle<sup>16</sup> was able to demonstrate a graded, age-adjusted linear increase in both SBP and DBP with increasing skin darkness among black men and women participating in the Charleston Heart Study. However, in 2 follow-up studies of this cohort, Keil et al<sup>17,18</sup> found no association between skin color and the incidence of hypertension after controlling for either education or other measures of social class. After adjusting for

known hypertension risk factors, Klag et al<sup>19</sup> found a positive linear relationship in both SBP and DBP only among black men and women of low socioeconomic status. Finally, Ernst et al<sup>20</sup> found a significant association between skin darkness and SBP in black men and women. This relationship did not persist when the results were stratified by gender, causing the authors to postulate that their findings were most likely an artifact of BP and skin color differences between men and women.

Three hypotheses may explain a positive dose-response relationship between BP and skin pigmentation. For the first, skin color is interpreted as a marker for the degree of black-white admixture. Implicit in this hypothesis are the following assumptions: (1) genes exist that predispose an individual to higher BP; and (2) the prevalence of these genes is higher among black than white individuals. The first assumption is based on empirical observations of higher BP among blacks than among whites.<sup>1</sup> Skin reflectance is a continuous measure of the degree of racial admixture between these populations,<sup>21</sup> and individuals with the darkest skin have the highest proportion of genes from a black population, including the genes that confer increased risk for high BP. One would expect, therefore, to observe higher BP associated with increased levels of skin pigmentation.

The applicability of this model to the Egyptian population is limited on both theoretical and empirical grounds. First, if genes for melanin regulation and BP were linked, successive matings within an admixed population would diminish a linkage disequilibrium after several generations. Admixture in Egypt has likely been occurring for many generations among many different racial groups, thereby increasing the likelihood of a dilution. Second, skin color in Egypt represents admixture among several racial groups, including dark-skinned individuals not of West African origin. Thus, the assumption that the prevalence of genes predisposing to high BP is higher in those with darker color skin may not be tenable, particularly in light of the fact that BP in the Egyptian Nubian population, an ethnic group with physical characteristics similar to those of black Africans, did not significantly differ from that of the nonblack study participants. Consequently, it is not clear whether the assumptions of the admixture hypothesis are tenable.

A second explanation of a relationship between melanin levels and BP is a direct physiological association. The regulation of both BP and melanin synthesis is under hormonal control, and neither is independent of other systems.<sup>22</sup> A mechanism of interaction, either through a specific gene product or a common metabolic intermediate, is not currently known.

Finally, a third explanation is confounding, namely, that skin color is associated with environmental factors known to influence BP. In our study, skin color was correlated with several variables that were independently associated with BP, including body mass, sodium-to-potassium excretion ratio (in women), and manual labor (in men), which one might consider a proxy for physical activity. However, in many but not all instances, the direction of the associations would tend to dilute a positive association between the Melanin Index and BP. For instance, darker-skinned women had lower BMIs

and lower sodium-to-potassium excretion values than their lighter-skinned counterparts. Thus, one might expect dark skin to be associated with low BP.

Skin color was also associated with socioeconomic measures. For both genders, darker-skinned individuals had lower levels of education than their lighter-skinned counterparts. Among males, higher education was associated with higher BP, while the association was in the opposite direction for females. However, education may be an unsatisfactory proxy for socioeconomic status in this population, particularly among women; additionally, it is prone to residual confounding. Cohort effects were observed in both genders; the average age within educational strata decreased as the level of education increased, suggesting that advanced schooling is a recent phenomenon.

Skin color was also associated with antihypertensive medication use. Lighter-skinned men and women with high BP were more likely to use medications and therefore were more likely to be excluded from the study than darker-skinned individuals with high BP. The positive relationship between skin color and BP in women is consistent with the direction of the bias that may have been introduced through differential exclusions with respect both to skin color and BP. Furthermore, the association between skin color and medication use suggests that access to health services, another proxy for socioeconomic status, was more available to lighter-skinned individuals.

In summary, this study documented a significant relationship between skin color and BP in women but not in men. While the relationship appeared to be independent of other known risk factors for hypertension, the concomitant association of skin color with such variables as BMI, sodium-to-potassium excretion ratios, manual labor, and medication use suggests that residual confounding may explain the apparent association.

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