Does life-course socioeconomic position influence racial inequalities in the occurrence of uterine leiomyoma? Evidence from the Pró-Saúde Study

A posição socioeconômica influencia as desigualdades raciais na ocorrência de miomas uterinos? Evidências do Estudo Pró-Saúde

¿El nivel socioeconómico influye en las desigualdades raciales en cuanto a la incidencia de miomas uterinos? Evidencia del Estudio Pró-Saúde

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Abstract

We aimed to investigate whether life-course socioeconomic position mediates the association between skin color/race and occurrence of uterine leiomyomas. We analyzed 1,475 female civil servants with baseline data (1999-2001) of the Pró-Saúde Study in Rio de Janeiro State, Brazil. Life-course socioeconomic position was determined by parental education (early life socioeconomic position), participant education (socioeconomic position in early adulthood) and their combination (cumulative socioeconomic position). Gynecological/breast exams and health insurance status were considered markers of access to health care. Hazard ratios (HR) and 95% confidence intervals (95%CI) were estimated using Cox proportional hazards models. Compared with white women, black and parda ("brown") women had higher risk of reporting uterine leiomyomas, respectively HR: 1.6, 95%CI: 1.2-2.1; HR: 1.4, 95%CI: 0.8-2.5. Estimates were virtually identical in models including different variables related to life-course socioeconomic position. This study corroborated previous evidence of higher uterine leiomyomas risk in women with darker skin color, and further suggest that life-course socioeconomic position adversity does not influence this association.

Leiomyoma; Race Relations; Socioeconomic Factors

Resumo

Nós investigamos se posição socioeconômica ao longo da vida medeia a associação entre cor/raça e ocorrência de mioma uterino. Analisamos 1.475 funcionárias públicas com dados na linha de base (1999-2001) do Estudo Pró-Saúde no Rio de Janeiro, Brasil. A posição socioeconômica ao longo da vida foi determinada pela escolaridade dos pais (posição socioeconômica precoce), escolaridade da participante (posição socioecônomica no inicio da vida adulta) e suas combinações (posição socioeconômica acumulada). Exames ginecológicos/mama e plano de saúde foram considerados marcadores de acesso à saúde. Razão de hazards *(RH) e intervalos de 95% de confiança (IC95%) foram estimados por modelos de riscos proporcionais de Cox. Comparadas às mulheres brancas, as de cor preta e parda tiveram maior risco de relatarem mioma uterino (RH: 1,6, IC95%: 1,2-2,1; RH: 1,4, IC95%: 0,8-2,5, respectivamente). As estimativas foram praticamente idênticas nos modelos que incluíram as diferentes variáveis de posição socioeconômica ao longo da vida. Este estudo corrobora evidências prévias de maior risco de mioma uterino entre mulheres de cor da pele mais escura e também sugere que a posição socioeconômica ao longo da vida não influencia esta associação.*

Leiomioma; Relações Raciais; Fatores Socioeconômicos

Introduction

Uterine leiomyomas, also called fibroid tumors, are the most common benign neoplasm of the female reproductive system. Their etiology is poorly understood, but sex steroid hormones are thought to influence their development and growth [1]. Although uterine leiomyomas have almost no association with mortality, they are related to a significant number of gynecological and obstetric problems affecting a woman's quality of life during her reproductive years [2]. As a result, uterine leiomyomas are the most common indication for hysterectomy [2,3,4].

In the United States, uterine leiomyomas occur two to nine times more often in black than in white women of all ages, and are associated with more serious symptoms in blacks, who are diagnosed at younger ages and have higher hysterectomy rates than whites [5,6,7,8,9,10,11]. The underlying mechanisms of this color/race inequality remain unknown. Established tumor risk factors, for example those tied to reproductive health (e.g. parity, age at first pregnancy, history of infertility, age at menarche, and contraceptive use), seem to explain only a small fraction of the race/color inequalities [5,6,8]. Alternative hypotheses, not yet explored in depth, point to an increase in polymorphisms and impaired regulation of hormonal receptors involved in the development of uterine leiomyomas [12,13], as well as vitamin D deficiency [14,15] and psychosocial stress [16,17], as potential high-impact causes of tumors in black women.

The role of socioeconomic position in these racial inequalities has also received little attention. Given that black women in many countries find themselves disproportionately disadvantaged in the social hierarchy, it is plausible to attribute these disparities, at least in part, to socioeconomic inequalities over the life course. Moreover, uterine leiomyomas is a slow-growing tumor that is diagnosed most often in women between 40 and 50 years of age, but can begin to develop a decade earlier [1]. For this reason, socioeconomic position markers from childhood and the beginning of adult life – time periods that most likely precede the onset of tumors – could help to clarify the color/race inequalities in uterine leiomyomas.

Empirical exploration of theoretical models from life course epidemiology could help us better understand these relationships [18,19,20,21]. According to life course models, health outcomes depend not only on exposure to risk factors, but also on individual lifespan and duration of exposure to those factors. Three such models have been developed: (1) a "critical period" or "sensitivity" model, (2) a social mobility model, and (3) a risk accumulation model. Under the first, socioeconomic position in early life influences health outcomes regardless of socioeconomic position in adulthood or other mediating factors. In the second, the focus is on socioeconomic position trajectories and associated health effects over the lifetimes of individuals. In the third, the gradual accumulation of exposures throughout life is what influences adult health [18,19,20,21].

It can be hypothesized that socioeconomic adversity throughout life could be a mediator of the relationship between color/race on the one hand, and influences on uterine leiomyomas on the other. Socioeconomic disadvantage could influence patterns of health behaviors related to uterine leiomyomas, sources of psychosocial stress, and more directly the deregulation of ovarian hormones. This influence could occur at specific times of life, such as the beginning of adulthood (critical period and/or sensitivity model), or it could be lifelong (social mobility model), causing the accumulation of different exposures among women of different racial groups (risk accumulation model).

To our knowledge, no studies have undertaken such an approach. Brazil possesses distinct characteristics for the conduct of such studies, as it has the largest black population outside of Africa, and marked socioeconomic and cultural diversity. In addition, unlike the United States, where origin and ancestry determine race, racial classification in Brazil is based on phenotypic characteristics, mainly skin color. As a result, racial identification tends to be more complex and fluid in the Brazilian context, resulting in the use of distinct terms to identify the skin color/race of the population [22]. Until now, information about uterine leiomyomas has been based on studies that analyzed the variable of race in a dichotomous way (white/non-white); Brazil's distinct perspective on matters of skin color/race could increase our understanding of the relationship between race and uterine leiomyomas.

This article presents the results of a study of color/race inequality in the self-reported history of uterine leiomyomas among Brazilian women participating in the longitudinal Pró-Saúde Study. Its principal objective was to investigate whether socioeconomic position – during childhood, at the beginning of adult life, and throughout the life course – mediates the association between skin color/race and a self-reported medical diagnosis of uterine leiomyomas.

Methods

Study population and data collection

The Pró-Saúde Study is a longitudinal study of civil servants at university campi located in the State of Rio de Janeiro, Brazil. Its principal focus is the investigation of social determinants of health and health behaviors [23].

The analyses in this article were conducted using cross-sectional data from participants enrolled at baseline. Eligible within the Pró-Saúde Study were 2,466 female workers, of whom 1,819 participated in both phases of the baseline study in 1999 and 2001 (73.8% of those eligible). Participants were excluded if they did not provide information about occurrence of uterine leiomyomas, age at diagnosis, or age at hysterectomy (n = 96); if they had a diagnosis of uterine leiomyomas or a hysterectomy before the age of 20 (n = 4); or if they did not provide information about one of the exposure variables (n = 235). In total, 1,475 participants were included in the current analyses.

Multi-dimensional questionnaires were administered by trained field workers and filled out by participants. Pilot studies, validation of scales, and reliability tests were carried out to assess the quality of information [23].

Variables

• Uterine leiomyoma

Ascertainment of uterine leiomyomas was based on the question, "*Has a doctor ever informed you that you had a uterine leiomyomas, a benign tumor in the uterus?*". The test-retest reliability of this information was evaluated over a two-week period among 98 individuals who were ineligible for the Pró-Saúde Study, but who were employees of the same university. Reliability was high (kappa = 0.94, or 95%CI: 0.86-1.00). Participants also provided information about their age at uterine leiomyomas diagnosis, whether that diagnosis was confirmed by a diagnostic ultrasound or histopathology report, and whether a hysterectomy was performed as a result.

• Skin color/race

Information about the participants' skin color/race was based on an open-ended question, "*In your opinion, what is your skin color or race?*". Forty-one distinct terms were registered by participants to self-identify participants' skin color/race [24]. Those terms were categorized into skin color/race: white, brown (e.g., "parda", "morena", "mulata", "mestiça", "cabocla"), black (e.g. "negra", "preta Africana", "escura"), and yellow. For the analyses in this article, yellow was excluded due to the small number of participants who reported being in this category (n = 8, 0.5%). More information can be found in Maio et al. [24].

• Markers of life course socioeconomic position

For information on childhood socioeconomic position, maternal and paternal educational levels were evaluated separately (less than primary education, primary education, secondary education or more). For socioeconomic position in early adult life, each participant's educational level was classified as primary education or less, secondary education, college or more. Cumulative socioeconomic position measures were also explored, considering separately (1) the father's and participant's education, and (2) the mother's and participant's education, by assigning a score of 0 to 2 for childhood socioeconomic position and for socioeconomic position in early adult life, with a score of 2 representing the highest level of disadvantage. Specifically, the scores were assigned as follows: childhood socioeconomic position (less than primary education = 2, primary education = 1, secondary education or more = 0); socioeconomic position in early adult life (primary education or less = 2, secondary education = 1, college or more = 0). The scores for each socioeconomic position variable were then added together to create a cumulative socioeconomic position score, ranging from 0 (most privileged) to 4 (most disadvantaged). The polichoric coefficient correlation between the ordinal variables of education used to compose the scores was 0.426 (participant and father) and 0.465 (participant and mother), showing no redundancy between variables. Previous studies on life course socioeconomic position and health outcomes have established similar scales [25,26]. Scores were categorized as "high" (0-1), "medium" (2), and "low" (3-4), for inclusion in categorical multivariate models.

Co-variates

• Markers of access to health care services

Pap smears and breast clinical exams (never done, done more than three years ago, or done within the past three years), as well as private health insurance status (yes, no), were analyzed.

Statistical analysis

Although the data were collected cross-sectionally, follow-ups were reconstructed from information reported by the participants.

Follow-up periods were defined as the time between 20 years of age and the age at data collection (1999) for the non-cases, and the age at uterine leimyomas diagnosis for the cases. Based on the natural history of uterine leimyomas development, women who were over the age of 50 at diagnosis were censored.

For bivariate analyses of color/race and uterine leimyomas, the Kaplan-Meier method was used; significance was determined by the log-rank and Peto tests [27]. Cox proportional risk models were used to estimate the multivariable-adjusted hazard ratios (HR) with 95% confidence intervals (95%CI).

Initially, two models were adjusted considering the following variables: skin color/race and age (model 1) and skin color/race, age, and variables assessing access to health care, including Pap smear, breast clinical exam, and private health insurance status (model 2). Five additional models were adjusted, with socioeconomic position variables included separately, in order to evaluate the possible influence of socioeconomic position on the association between race and uterine leimyomas. Results from each model were compared to those of model 2. Schoenfeld residuals were used to test the proportional odds assumption.

Sensitivity analyses were conducted to evaluate the possibility of misclassification due to a self-reported outcome. First, to reduce the possibility of false positives, three subsets of cases were excluded from these analyses: (a) cases of uterine leimyomas with no ultrasound or histopathology diagnostic confirmation; (b) cases that were asymptomatic at diagnosis; and (c) cases that did not require hysterectomy (in this case we used age at hysterectomy instead of age at diagnosis to delimit the period of follow-up). Second, to reduce the possibility of false negatives, participants younger than 30 were excluded from the sensitivity analyses.

Data entry and consistency checks were carried out using Epi Info (Centers for Disease Control and Prevention, Atlanta, USA), and the statistical analyses were executed with the program R, version 2.6.2 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org). The study was approved by the Ethics Research Committee at the State University of Rio de Janeiro.

Results

Over half of the women (54.7%) reported their skin color/race as white. Brown and black skin colors/races were reported by 22.7% and 22.6%, respectively. Participants' ages ranged from 22 to 67 years (average, 40 years). Average ages were 38.9 for white women, 40.7 for brown women, and 41.8 for black women.

Table 1 shows the distribution of variables under study according to participants' skin color/race. Black women as a group had the worst socioeconomic position profile and the lowest proportion with private health insurance. The proportions of socioeconomic position variables and private health insurance for brown women were between those of blacks and those of whites. All three groups had high proportions of participants who had a Pap smear or a breast exam by a gynecologist in the previous three years, with whites having slightly higher proportions of that history than black and brown women (though the difference was not statistically significant) (Table 1).

Table 2 shows the distribution of study variables according to frequency of uterine leiomyomas. Tumors were more frequent among black women and among those with the worst socioeconomic conditions (lowest levels of education, parental education and lifelong socioeconomic position). Uterine leiomyomas were also more common among women who reported undergoing a breast clinical exam and a Pap smear in the previous three years (Table 2).

Figure 1 shows the cumulative risk curves for incidence of self-reported diagnosis of uterine leiomyomas according to skin color/race. Overall, the lowest incidence of uterine leiomyomas occurred among white women, followed by brown women and black women. However, at finer calibrations the pattern is not as clear. Between approximately 20 to 25 follow-up years, white women have a lower cumulative incidence than brown women. But the cumulative incidence at the end of the follow-up is the same in whites and browns (Figure 1).

Table 3 shows hazard ratios for uterine leiomyomas according to skin color/race for seven models adjusted for age, socioeconomic position, and variables related to access to health care services. It also shows the same associations after exclusion (sensitivity analyses) of asymptomatic cases of diagnosed uterine leiomyomas (which were: 10.4% for whites, 15.4% for browns and 22.9% for blacks – not shown in table), as well as cases that did not require hysterectomy (4.9% for whites, 7.8% for browns and 17.3% for blacks – not shown in table). Compared with

Table 1

Distribution of study variables according to participants' skin color/race. Pró-Saúde Study, Rio de Janeiro, Brazil (1999-2001).

	White n (%)	Brown n (%)	Black n (%)	p-value *
Age (mean, SE)	38.9 (8.1)	40.7 (8.0)	41,8 (8.1)	< 0.001 **
Childhood socioeconomic position (paternal educational attainment)				
Secondary education or more	323 (40.1)	94 (28.1)	53 (15.9)	< 0.001
Primary education	205 (25.4)	82 (24.5)	87 (26.1)	
Less than primary education	278 (34.5)	159 (47.5)	193 (58.0)	
Childhood socioeconomic position (maternal educational attainment)				
Secondary education or more	262 (32.5)	52 (15.5)	24 (7.2)	< 0.001
Primary education	215 (26.7)	87 (26.0)	82 (24.6)	
Less than primary education	329 (40.8)	196 (58.5)	227 (68.2)	
Early adult life socioeconomic position (participant educational attainment)				
College or more	502 (62.3)	121 (36.1)	101 (30.3)	< 0.001
Secondary education	236 (29.3)	140 (41.8)	143 (42.9)	
Primary education or less	68 (8.4)	74 (22.1)	89 (26.7)	
Cumulative socioeconomic position (paternal and participant educational attainment)				
High	439 (54.5)	112 (33.4)	74 (22.2)	< 0.001
Medium	204 (25.3)	91 (27.2)	99 (29.7)	
Low	163 (20.2)	132 (39.4)	160 (48.0)	
Cumulative socioeconomic position (maternal and participant educational attainment)				
High	388 (48.1)	93 (27.8)	54 (16.2)	< 0.001
Medium	240 (29.8)	86 (25.7)	103 (30.9)	
Low	178 (22.1)	156 (46.6)	176 (52.9)	
Private health insurance				
Yes	599 (74.3)	201 (60.0)	150 (45.0)	< 0.001
No	207 (25.7)	134 (40.0)	183 (55.0)	
Pap smear				
Within the past 3 years	727 (90.2)	295 (88.1)	288 (86.5)	0.167
Never/More than 3 years ago	79 (9.8)	40 (11.9)	45 (13.5)	
Breast clinical exams				
Within the past 3 years	727 (90.2)	294 (87.8)	288 (86.5)	0.154
Never/More than 3 years ago	79 (9.8)	41 (12.2)	45 (13.5)	

SE: standard error.

* p-value derived from Pearson's chi-squared test for categorical variables;

** p-value derived from ANOVA test.

white women, black women had a greater risk of developing uterine leiomyomas, independently of the variables entered in the different models. Differences between white and brown women were not statistically significant. Regardless of the socioeconomic position variables adjusted for, the HR comparing blacks and whites was 1.7 and statistically significant. These hazard ratios were further away from 1.0 following exclusion of cases of asymptomatic self-reported diagnosed uterine leiomyomas and cases that did not require hysterectomy.

The results of other sensitivity analyses (selective exclusion of participants younger than 30 years of age and those whose diagnosis of uterine leiomyoma was not confirmed by ultrasound or a histopathology report) were virtually identical to the overall analyses (not shown in table). Schoenfeld residuals demonstrate that all analyzed variables displayed constant risk differences over time.

Table 2

Distribution of study variables according to frequency of uterine leiomyoma. Pró-Saúde Study, Rio de Janeiro, Brazil (1999-2001).

	Uterine leiomyoma		p-value *
	n	(%)	
Skin color/race			
White	146	18.1	< 0.001
Brown	74	22.1	
Black	107	32.1	
Childhood socioeconomic position (paternal educational attainment)			
Secondary education or more	86	18.3	0.032
Primary education	84	22.5	
Less than primary education	157	24.9	
Childhood socioeconomic position (maternal educational attainment)			
Secondary education or more	62	18.3	0.033
Primary education	78	20.3	
Less than primary education	187	24.9	
Early adult life socioeconomic position (participant educational attainment)			
College or more	152	21.0	< 0.001
Secondary education	100	19.3	
Primary education or less	75	32.5	
Cumulative socioeconomic position (paternal and participant educational attainment)			
High	123	19.7	0.022
Medium	83	21.1	
Low	121	26.6	
Cumulative socioeconomic position (maternal and participant educational attainment)			
High	103	19.3	0.025
Medium	91	21.2	
Low	133	26.1	
Private health insurance			
Yes	209	22.0	0.870
No	118	22.5	
Pap smear			
Within the past 3 years	301	23.0	0.049
Never/More than 3 years ago	26	15.9	
Breast clinical exams			
Within the past 3 years	305	23.3	0.005
Never/More than 3 years ago	22	13.3	

* p-value derived from Pearson's chi-squared test for categorical variables.

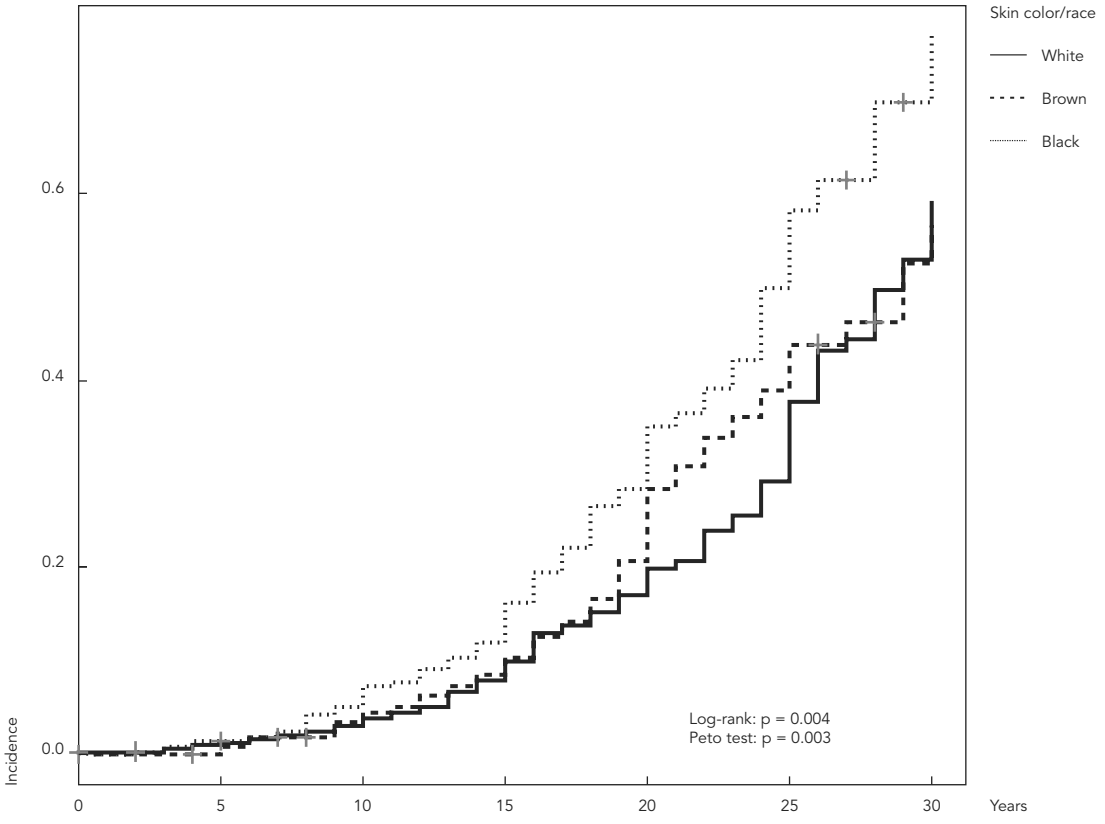
Discussion

To the authors' knowledge, this is the first epidemiological study evaluating the role of life course socioeconomic position in the association between uterine leiomyomas and black or brown skin color/race. Black women had a statistically significant higher likelihood of reporting a diagnosis of uterine leiomyomas than their white counterparts; brown women's risks fell between those of blacks and whites. Differences between white and brown women, however, were not statistically significant.

These results are consistent with previous studies in the United States, in which black women were found to have a higher risk of uterine leiomyoma than white women. Marshall et al. [6] found a relative risk of uterine leiomyomas

Figure 1

Cumulative risk curves (Kaplan-Meier) and p-values from log-rank and Peto tests for medical diagnosis of self-reported uterine leiomyoma according to skin color/race. Pró-Saúde Study, Rio de Janeiro, Brazil (1999-2001).



of 3.3 (95%CI: 2.7-3.9) and of hysterectomy due to uterine leiomyomas of 1.9 (95%CI: 1.2-2.8) among black compared to white women, following adjustments for variables such as age, body mass index (BMI), time elapsed since last pregnancy, history of infertility, alcohol consumption, tobacco use, physical and leisure activity, age at menarche, age at first pregnancy, contraceptive use, and marital status [6]. Faerstein et al. [5] reported that, compared with white women, black women had more than nine times the odds of uterine leiomyomas (OR = 9.4; 95%CI: 5.7-15.7) after adjustment for age at menarche, use of oral contraceptives, tobacco use, BMI, hypertension, diabetes mellitus, and history of pelvic inflammatory disease. Baird et al. [8] found a uterine leiomyomas odds ratio for blacks versus whites of 2.7 (95%CI: 2.3-3.2) after adjustment for BMI and parity.

While previous studies have analyzed skin color/race as a dichotomous variable (white/non-white or white/black), we used three categories. In contrast with the United States, for example, racial/ethnic classification in Brazil is based on phenotypic characteristics, such as skin color, which allows for a variety of categories. Currently, there are three ways of categorizing race in Brazil that are worth emphasizing: (1) that of the Brazilian census, which distinguishes among five discrete categories of skin color – white, brown, black, Asian ("yellow"), and Native Brazilian ("indigenous"), the fifth of which considers ancestry and ethnicity differently from the other four; (2) that of popular discourse, which uses a diverse

Table 3

Hazard ratios (HR) expressing the relationship of skin color/race to medical diagnosis of self-reported uterine leiomyoma, adjusted for lifecourse socio-economic position variables, and access to and use of health care services *. Pró-Saúde Study, Rio de Janeiro, Brazil (1999-2001).

Model	Medical diagnosis of uterine leiomyoma	Sensitivity analysis	
		Exclusion of asymptomatic cases	Exclusion of cases with no hysterectomy
	HR (95%CI) [n = 1,475]	HR (95%CI) [n = 1,328]	HR (95%CI) [n = 1,245]
Model 1 (age)			
White	1.0	1.0	1.0
Brown	1.1 (0.9-1.5)	1.4 (1.0-2.1)	1.4 (0.8-2.5)
Black	1.6 (1.2-2.1)	2.0 (1.4-2.8)	2.6 (1.7-4.0)
Model 2 (age and access to health care) **			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.5 (1.0-2.1)	1.6 (0.9-2.7)
Black	1.7 (1.3-2.2)	2.0 (1.4-2.8)	2.8 (1.7-4.4)
Model 3 (Model 2 + paternal educational attainment)			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.4 (1.0-2.1)	1.6 (0.9-2.7)
Black	1.7 (1.3-2.2)	2.0 (1.4-2.8)	2.7 (1.7-4.3)
Model 4 (Model 2 + maternal educational attainment)			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.4 (1.0-2.1)	1.5 (0.8-2.5)
Black	1.7 (1.3-2.3)	2.0 (1.4-2.8)	2.5 (1.5-3.9)
Model 5 (Model 2 + participant educational attainment)			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.4 (1.0-2.1)	1.6 (0.9-2.8)
Black	1.7 (1.3-2.3)	2.0 (1.4-2.8)	2.8 (1.8-4.5)
Model 6 (Model 2 + cumulative socioeconomic position – paternal and participant educational attainment)			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.4 (1.0-2.1)	1.6 (0.9-2.7)
Black	1.7 (1.3-2.2)	1.9 (1.3-2.7)	2.7 (1.7-4.3)
Model 7 (Model 2 + cumulative socioeconomic position – maternal and participant educational attainment]			
White	1.0	1.0	1.0
Brown	1.2 (0.9-1.6)	1.4 (1.0-2.0)	1.5 (0.9-2.6)
Black	1.7 (1.3-2.2)	1.9 (1.3-2.7)	2.6 (1.6-4.1)

* Follow-up periods were defined as the time between 20 years of age and the age at data collection (1999) for the non-cases, and the age at diagnosis for the cases;

** Variables for health care access: Pap smear, clinical breast exam, and private health insurance status.

nomenclature [24]; and (3) that of black political activists, who defend the use of the category "negro" or "of African descent" rather than "brown" and "black". The objective of the latter classification system is to reestablish the identification of ancestry, and consequently of collective identity, among African descendants in Brazil [22]. Results from this study, however, point to differences between brown and black women, which reinforce the need to consider these distinct racial categories in health research in societies like Brazil's. On the one hand, the lack of statistical differences between white and brown women might indicate the presence of similar risk factors for these groups; on the other hand, the same lack of statistical difference may show that women with similar phenotypes placed themselves in distinct color/racial groups, a finding which would confirm the notion of the fluidity of the color/race construct in Brazilian society [28,29].

Another finding of this study was the strengthening of the racial gradients when cases of asymptomatic uterine leiomyomas, and those that did not require hysterectomy, were excluded. These results, the product of sensitivity analyses, may indicate a greater risk of more clinically severe tumors in black women. Alternative possible explanations include increased medical surveillance among blacks, or perhaps racial discrimination among health professionals in deciding or administering treatment [30]. For example, in some studies nonwhite women overall had lower rates of Pap smears and of anesthesia use in vaginal delivery, and a higher risk of surgical sterilization, independently of other socio-demographic characteristics [31,32,33].

In this study, despite the inverse association between socioeconomic position and uterine leiomyomas, as well as between socioeconomic position and black color/racial identification, several adjustments for socioeconomic position markers did not change the associations, suggesting that socioeconomic position is not a mediator of the relationship between color/race and uterine leiomyomas. Few studies address associations between socioeconomic position and uterine leiomyomas, which makes it difficult to compare this study's results with the epidemiological literature. Most etiological studies analyze proximal factors in the uterine leiomyomas causal chain, in general associated with hormonal deregulation, but do not address social determinants. Thus, variables such as education have been analyzed [34,35,36,37,38] as potential confounders, but have not been the central focus of analysis. Still, some studies observed no association [8,39,40,41] between education and uterine leiomyomas, while one found a direct association [42]. Two studies have addressed the association between tumors and low levels of parental education, food insecurity, and low income in childhood, and found direct associations only among whites [43,44].

However, some methodological aspects of our study may have influenced these findings. Although information about the education marker for socioeconomic position covered more than one time period in participants' life course, this marker most likely does not fully capture the complexity of social stratification and resulting lifelong, socially patterned exposures and behaviors [45,46,47]. In addition, this marker may not be equivalent across color/race groups, again for complex social, economic and political reasons [46,47]. In the United States, for example, there are great differences in the quality of education enjoyed by whites and blacks; moreover, the incomes of individuals of similar educational level were higher among whites than among blacks and Hispanics [45,48,49]. Nonetheless, education is a widely utilized measure of an individual's location in the social hierarchy. Higher levels of education provide better opportunities for jobs and higher wages, which lead to better nutrition, housing, and access to health services. Higher educational attainment also strengthens cognitive resources that influence health-related decisions and behaviors [46,50,51]. Parental education level, in turn, is a widely used indicator of childhood socioeconomic position, and is a powerful clue to the environment in which the child grows, learns, and adopts behaviors that may influence his or her future life [50].

If life course socioeconomic position does not mediate the uterine leiomyomas-color/race association, alternative hypotheses must be discussed even though they were not objects of empirical exploration in this study. Sources of psychosocial stress throughout a woman's life (which may or may not be influenced by life course socioeconomic position) may be a link in the causal chain. For example, a study of black women in the U. S. showed that increased exposure to racial discrimination may be associated with uterine leiomyomas via allostatic load [52]. In addition, recent studies have demonstrated that physical and sexual abuse during childhood or adolescence may be associated, in a graded pattern, with higher uterine leiomyomas risk, and that parental emotional support may buffer the impact of that abuse. These studies have found that severe stress in early life is associated with deregulation of the hypothalamic-pituitary-adrenal (HPA) stress pathway, and may affect ovarian hormone synthesis and uterine leiomyomas growth. This autonomic stress response may persist into adulthood [53,54].

Other biological mechanisms may also be involved. Women with darker skin color tend to have lower levels of circulating vitamin D, which may be a risk factor for the development of uterine leiomyomas [14,15,55]. In addition, cytogenetic studies have found similarities between the structural organization of uterine leiomyomas and that of keloids – overgrowths of scar tissue that increase the production of extracellular matrix proteins during the scarring process [56] – also associated with elevated melanin levels [57] and vitamin D deficiency [58]. The investigation of such biological mechanisms, possibly resulting from phenotypic features, would not mean an endorsement of genetic inheritance as the basis for racial classifications. The wide variability of humans' external physical characteristics, commonly used to describe racial groups, seems to reflect changes and adjustments, over the mil-

lennia, to variations of climate and other environmental factors, as well as historical and social conditions [22,59,60,61].

Two methodological choices by the authors should be mentioned. First, we prioritized the study of distal variables in the causal chain. We therefore chose not to include in the analysis proximal or intermediate variables (known risk factors) such as those related to lifestyle and reproductive health. We believed that to include such variables, while tempting as a route of investigation, would complicate the relationships among color/race, socioeconomic position and uterine leiomyomas, and might reduce or even eliminate the main association of interest, hindering the understanding of these very relationships.

Our other choice was to use Cox models in multivariate analyses. This decision was made because the study had collected data on participant age at uterine leiomyomas diagnosis. Therefore, a "follow-up" period could be estimated, and our analyses could then be used as alternatives to cross-sectional analysis, which necessarily disregards the distribution of time that each participant contributed to the study.

Among our study's limitations is the use of self-reported information regarding tumor diagnosis. Because many uterine leiomyomas cases are asymptomatic, diagnosis depends on access to and utilization of health care services. When participants did not have access to a diagnosis, they may report their illness inaccurately, and the resulting associations may be underestimated. We implemented two specific strategies to reduce the likelihood of these biases. The first, albeit indirect, was to assess the reliability of the question about diagnosis of uterine leiomyomas. That reliability proved to be excellent. Second, analyses were conducted following the selective exclusion of cases lacking a confirmatory diagnosis of uterine leiomyomas by way of ultrasound or histopathology report, as well as cases in women under 30 years of age. Our estimates remained unchanged in each of these situations.

Other biases potentially associated with cross-sectional studies may have influenced our results. First, certain hypothesized risk factors for uterine leiomyomas, such as those related to atherogenesis [57], may also be associated with color/race. As such, an increase in premature mortality among black and brown women could dilute the associations among the women who survived. The population under study, however, can be considered to be young (average age 40 years), which makes this explanation less likely. Second, although Pap smears and breast exams were used as markers of access to health care services, a residual bias may exist in which the exams performed on white women were of higher quality, even though they had the same frequency; this may also have diluted the strength of the associations we observe. Conversely, if the exams were of higher quality among black women than white women, our results could be overestimated.

In summary, the observation of a higher occurrence of uterine leiomyomas in women with darker skin color in a Brazilian sample is consistent with findings from U.S. studies. The results also suggest that life course socioeconomic position does not mediate this association, a possibility that had not been explored in previous studies.

Much remains to be understood about the ways in which social exposures are related to biological mechanisms that affect the development of outcomes like uterine leiomyomas. Future epidemiologic studies should be longitudinal in nature, and should include additional markers of socioeconomic position. The color/race inequalities found in our study suggest that further research should evaluate both biological and environmental exposures, such as the role of vitamin D deficiency and sources of psychosocial stress, including experiences of racial discrimination among black women, as potential explanatory factors for the color/race-uterine leiomyomas relationship.

Resumen

Hemos investigado si es estatus socioeconómico durante toda la vida influye en la asociación entre raza y presencia de mioma uterino. Se analizaron a 1.475 funcionarias, con datos provenientes de la cohorte Pró-Saúde (1999-2001) en Río de Janeiro, Brasil. La posición socioeconómica durante toda la vida se determinó por la educación de los padres (posición socioeconómica temprana), educación de la participante (posición socioeconómica principio de la edad adulta) y combinaciones de los mismos (posición socioeconómica acumulada). Exámenes ginecológicos/mama y el plan de salud se consideran marcadores de acceso a la salud. La razón de riesgo (hazards ratio, HR) y el intervalo de un 95% de confianza (IC95%) se calcularon utilizando modelos de riesgos proporcionales. La comparación entre mujeres blancas, negras y mulatas/mestizas concluyó que tenían un riesgo más elevado de mioma uterino, en los siguientes porcentajes respectivamente HR: 1,6 IC95%: 1,2-2,1; HR: 1,4 IC95%: 0,8-2,5. Las estimaciones fueron prácticamente idénticas en los modelos que incluyen diferentes variables de posición socioeconómica para toda la vida. Este estudio apoya la evidencia de mayor riesgo de mioma uterino entre mujeres de color de piel más oscuro y también sugiere que la posición socioeconómica para toda la vida no influye en esta asociación.

Leiomioma; Relaciones Raciales; Factores Socioeconómicos

Contributors

All authors collaborated to the conception, analyses and writing of this review article and approved the final version.

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