Published in final edited form as:

Am J Obstet Gynecol. 2008 February ; 198(2): 168.e1–168.e9.

The Impact of Race as a Risk Factor for Symptom Severity and Age at Diagnosis of Uterine Leiomyomata among Affected Sisters

Karen L. HUYCK, M.D., Ph.D., M.P.H.¹, Carolien I.M. PANHUYSEN, M.D., Ph.D.², Karen T. CUENCO, Ph.D.², Jingmei ZHANG, M.S.², Hilary GOLDHAMMER, M.S.³, Emlyn S. JONES, M.D., M.P.H.³, Priya SOMASUNDARAM, M.B.B.S.³, Allison M. LYNCH, B.S.³, Bernard L. HARLOW, Ph.D.⁴, Hang LEE, Ph.D.⁵, Elizabeth A. STEWART, M.D.³, and Cynthia C. MORTON, Ph.D.^{3,6}

¹Department of Pathology, University of Vermont, Burlington, Vermont ²Genetics Program, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts ³Departments of Obstetrics, Gynecology, and Reproductive Biology and ⁶Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts ⁴Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts ⁵Massachusetts General Hospital Biostatistics Center, Harvard Medical School, Boston, Massachusetts

Abstract

Objectives—To identify risk factors for uterine leiomyomata (UL) in a racially diverse population of women with a family history of UL and to evaluate their contribution to disease severity and age at diagnosis.

Study Design—We collected and analyzed epidemiological data from 285 sister pairs diagnosed with UL. Risk factors for UL-related outcomes were compared among black (n=73) and white (n=212) sister pairs using univariate and multivariate regression models.

Results—Black women reported an average age at diagnosis of 5.3 years younger (SE 1.1, p<0.001) and were more likely to report severe disease (OR=5.22, CI 95% 1.99–13.7, p<0.001) than white women of similar socioeconomic status.

Conclusions—Self-reported race is a significant factor in the severity of UL among women with a family history of UL. Differences in disease presentation between races likely reflect underlying genetic heterogeneity. The affected sister-pair study design can address both epidemiological and genetic hypotheses about UL.

Keywords

Uterine leiomyomata; fibroids; family study; racial differences; symptom severity

* Please address correspondence to: Cynthia C. Morton, Ph.D., Departments of Obstetrics, Gynecology, and Reproductive Biology and Pathology, Brigham and Women's Hospital, 77 Avenue Louis Pasteur, HNRB Room #160, Boston, MA 02115, (617) 525-4535 (phone), (617) 525-4533 (fax), cmorton@partners.org.

Condensation

Symptom severity and age at diagnosis of uterine leiomyomata are strongly associated with race in women with a family history of uterine leiomyomata.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

Uterine leiomyomata (UL), also known as fibroids, are the most common pelvic tumors in women. Frequent symptoms include prolonged and profuse menstrual bleeding, pelvic pain, and reproductive dysfunction.¹ Although important advances in surgical and medical management have provided new alternative treatments for women with UL, the profound morbidity of these tumors accounted for over one-third of hysterectomies performed in the U.S. from 1994 to 1999 and for over 2.1 billion dollars in direct health care costs in 2000.^{2–4} For abundant reasons, including medical, psychological, and interest in preserved fertility, hysterectomy remains an undesirable endpoint for many women.

Despite the major public health impact of UL, underlying causes of their development and growth remain largely unknown. Molecular and epidemiological studies suggest that genetic factors influence UL development and growth.^{5–10} However, there is limited or no information regarding susceptibility genes or risk factors among women with a family history of UL.¹¹ Identified risk factors for development of UL in the general population include age, African descent, pre-menopausal status, early menarche, oral contraceptive use, obesity, nulliparity, current alcohol consumption, and diet high in red meat, although not all studies have shown consistent association of UL with these factors.^{12–14}

The effect of race on incidence and severity of UL is particularly notable. After controlling for BMI and other known risk factors, black women experience a higher incidence and relative risk of UL than other racial and ethnic groups including white, Hispanic, and Asian women.¹⁵ Black women also tend to have more severe disease than white women, including an earlier age at diagnosis and at hysterectomy, a higher hysterectomy rate, and larger and more numerous tumors.¹⁶

These differences in UL incidence and severity between white and black women may be due to genes conferring increased risk of poor UL outcomes. Controlling for family history of UL as a proxy for elevated genetic risk could reduce the racial difference in UL disease outcomes. Therefore, it is important to determine whether risk factors among individuals with a family history of UL differ from risk factors identified in the general population.

To date, no study has examined UL epidemiology in women with a family history of UL. We describe here epidemiologic data from sisters with UL (collected with the long term goal of correlating these data with genetic studies) and assess differences among black and white sisters with respect to medical, exposure, and lifestyle variables. In the first analysis of this ongoing family study, we examine the relationship of symptom severity and age at diagnosis with race in women with UL who have at least one sister with UL.

Materials and Methods

Human Research Subjects

Subjects were affected sister-pair participants from the ongoing “Finding Genes for Fibroids” study, a genetic study to identify susceptibility genes for UL (www.fibroids.net). Sister pairs comprised a proband and one sister, both with UL or a documented history of UL. In the case of probands with more than one affected sister, only the sister closest in age to the proband was included in the analysis. Participants were recruited domestically and internationally by collaborating physicians, by advertisements and articles in general interest publications, by pamphlets distributed nationally at participating clinics, conferences, and health fairs, by flyers posted in appropriate public venues, by newsletters mailed to active participants and other interested individuals, and via the web site for the Center for Uterine Fibroids (www.fibroids.net).

Probands initially completed a screening questionnaire about family medical history. Eligible probands and family members were then asked to complete a detailed questionnaire on personal risk factors. This second questionnaire was adapted from the “Cancer Risk and Prevention Questionnaire, Breast and Ovary” survey from the Brigham and Women’s Hospital Obstetrics and Gynecology Epidemiology Center and included questions about racial background, demographics, environmental exposures, life style, diet, medication and supplement use, medical history, gynecologic history, and pregnancy history. All subjects provided informed consent before completing study procedures. All study procedures and materials were reviewed and approved by the Human Research Committee of Partners HealthCare System.

Confirmation of UL diagnosis was determined through medical records for 520 of 570 (91%) of study participants. Sister pairs with Mendelian-inherited UL-related syndromes, Reed (MIM150800) or Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) (MIM605839) syndromes, were identified by clinical history and excluded from this study. Monozygotic twins, individuals with internally inconsistent questionnaire responses, and women who self reported that they were half-sisters also were excluded.

Because disease severity is an important measure of genetic contribution and no classification system exists for this disease, we created an algorithm at the outset of the study encompassing variables easily addressed by questionnaire that appeared likely to confer more severe disease. Participants were classified as severely or not severely affected based on early age at diagnosis, severity of symptoms during a typical menstrual cycle with UL, and history of UL-related surgeries (Figure 1).

Race was classified according to the National Institutes of Health guidelines. Women who reported their racial background as “African-American,” “African,” “West Indian,” “Caribbean,” or “Afro-Caribbean” were considered of black race. Women who reported their racial background as “White (non-Hispanic),” “European,” and “Middle Eastern” were considered of white race. Sister pairs with discordant self report of race and women of Hispanic, Asian, or other racial or ethnic origin were excluded from this analysis because of difficulty in categorization or because of small sample size.

Analysis

Descriptive statistics (e.g., means, medians, and percentages) of demographic factors and of potential risk factors were calculated for all participants. Univariate comparisons of risk factors were performed using two-sample t, Wilcoxon rank sum, and Fisher’s exact tests as appropriate. Regression modeling was performed among probands with UL to assess the association between primary outcomes of interest (e.g., symptom severity and age at diagnosis) and race, and potential confounders. Including only probands in the regression analyses avoided confounding by familial correlation. For each outcome, three models were evaluated. Model 1 included only race (black or white) as a predictor. Model 2 included race as a predictor and only confounders identified as significant ($p \leq 0.05$) through initial screening using univariate regression. Model 3 included all potential confounders. Confounders were assessed by evaluating regression estimates for race, the primary predictor of interest, from all three models. A variable was considered a confounder if the race regression coefficient or its standard error changed 10% or more between models with and without the variable. Data were analyzed using the SAS System for Windows software program (release 9.1, SAS Institute, Cary, NC).

Results

Of 570 participants (285 sister pairs) who met eligibility criteria and were included in the analysis, 546 (96%) were from the U.S. and 24 (4%) were recruited from other countries including Australia, Barbados, Canada, France, Romania, Spain, Switzerland, the United

Kingdom, and the West Indies. Of U.S. participants, 215 (39%) were from the Northeast, 27 (5%) from the Northwest, 80 (15%) from the Midwest, 77 (14%) from the Southwest, and 147 (27%) from the South.

Of 285 sister pairs included in the analysis, 73 were black (26%) and 212 were white (74%). Twenty-three sister pairs were excluded prior to analysis because of inconsistent race reporting. Thirty-eight participating families included more than one affected sister: 25 white women and six black women enrolled in the study with two sisters, six white women enrolled with three sisters, and one white woman joined the study with four sisters.

Table 1 shows demographics of the study population and risk factors for UL by race. Black participants were significantly younger than white participants (40.8 ± 6.1 versus 45.1 ± 8.1 years, $p < 0.001$), had an earlier age of menarche ($p < 0.001$), were more likely to be obese ($p < 0.001$), and were less likely to have a history of smoking ($p = 0.004$). Percentage of participants with a college degree or higher was similar between races ($p = 0.51$). Black and white participants had no significant difference in OCP use or history of pregnancy. There was no significant racial difference in the percent of participants performing regular vigorous exercise; however, a greater percentage of white than black participants exercised more than three hours weekly ($p = 0.02$).

Table 2 shows dietary factors by race. Black participants reported significantly lower dietary intake of red meat, fruit, vegetable, milk, coffee, tea, chocolate, red wine, liquor, and beer than white participants. Overall, black participants were less likely to drink alcohol than white participants ($p = 0.03$). Black and white participants did not report significantly different decaffeinated coffee, white wine, or egg consumption (data not shown).

Table 3 presents UL characteristics by race. Black participants had a significantly younger age at diagnosis of UL ($p < 0.001$), fewer days between periods ($p < 0.001$), and more severe menstrual pain ($p < 0.001$) than white participants. No significant racial difference was observed between method of UL diagnosis, predictability of cycle, history of hysterectomy or other UL-related surgery, or time since UL diagnosis. All participants who reported hysterectomies had hysterectomies that were UL-related. Forty-six participants (four black women and 42 white women) reported having had natural menopause not due to hysterectomy or other known reasons.

Similar results were found when probands and their sisters were analyzed separately (data not shown). The mean age of probands was two years younger than that of their participating sisters (43 ± 7.9 versus 45 ± 7.8 years, $p = 0.04$); however, the mean age of UL diagnosis was similar for probands and sisters (35.7 ± 8.2 versus 35.7 ± 8.0 years, $p = 0.99$). The majority of participants had a college degree or higher (85% of probands and 80% of sisters). In contrast to analyses of probands only, analyses of sisters only detected no significant difference in menstrual pain (19% of black sisters and 19% of white sisters reported severe pain, $p = 0.89$).

Black participants were significantly more likely to meet our criteria for severe disease than white participants (91.1% versus 71.5%, $p < 0.001$) (Table 4). Logistic regression analyses demonstrated that race remained associated with severity after adjusting for known UL risk factors including BMI, age of menarche, history of smoking, OCP use prior to 20 years of age, history of pregnancy, current alcohol use, and red meat consumption (OR=5.22, CI 95% 1.99–13.7, $p < 0.001$) (Table 5). Similarly, black probands were an average of six years younger at diagnosis of UL than white probands ($\beta = -6.00$, SE(β) 1.1, $p < 0.001$) (Table 6). Including the significant confounders, history of pregnancy and age at menarche, in the model changed the estimate for race to 5.3 years younger at diagnosis of UL. The average age at UL diagnosis was delayed by almost one year for every one year increase in age of menarche, while the

average age at diagnosis for women without a history of pregnancy was three years younger than women with a history of pregnancy.

Regression analyses stratified by race did not reveal additional insights into possible differential contribution of risk factors to the presentation of UL between black and white probands, most likely because the population of black women lacked sufficient statistical power ($n=58$). When white women were analyzed separately, however, results revealed that women without a history of pregnancy were diagnosed with UL an average of almost four years younger than women with a history of pregnancy ($\beta=-3.85$, $SE=1.24$, $p=0.002$; data not shown). Of note, there was no change in the results when the regression analyses were repeated using only US participants.

Comment

This is the first description and analysis of a large population of sibling pairs affected with UL. This study was designed both for traditional epidemiologic risk factor assessment in a genetically related population and for assessing genotype-phenotype relationships in a genome-wide scan for UL susceptibility genes. Even compared to white women with affected siblings, black women have more than five times higher odds of having severe UL symptoms and develop disease five to six years earlier.

The change from six years difference in age at diagnosis between black and white women reported in Table 3 to five years reported in the regression model is likely the result of confounding by 'age at menarche' and 'history of pregnancy.' For every one year increase in 'age at menarche', the diagnosis of UL was postponed by a year. This suggests that the time interval between menarche and onset of UL, rather than the age at menarche itself, is a disease characteristic. The finding that women without a history of pregnancy were on average three years younger at age of diagnosis than women with a history of pregnancy may suggest that early UL diagnosis is an indicator of more severe UL causing infertility in these individuals. Alternatively, women who have been pregnant may have an exposure that delays the progression or severity of UL symptoms. The current study cannot clarify which of these mechanisms may underlie the observations.

We observed a difference in pain reporting between sisters and probands. This difference may reflect probands with more discomfort and motivation to seek health information and enroll in our study, versus sisters who may have enrolled because they were recruited by the probands and not because they had particularly severe symptoms. We also found that black participants had markedly different dietary habits from white participants. Whether the dietary differences between the black and white women found in our study contribute to UL growth and development is an interesting hypothesis that would require further investigation.

We are aware that the data presented are not representing a general population sample, however, our population of affected sister pairs has a similar racial distribution of risk factors, including history of pregnancy, smoking, age of menarche, and menopausal status, as previously reported UL populations.^{15, 16} In addition, our population is comparable to the general U.S. population with respect to age at menarche, BMI, and smoking. For example, our data are consistent with published national data showing an earlier age of menarche and higher BMI in black women compared to white women.^{17, 18} Smoking rates in our population also are consistent with national trends; white women in the U.S. are more likely to smoke than African American women (20% versus 18%), and the percent of smokers among individuals with college and graduate degrees in the U.S. is estimated to be 12% and 8%, respectively.¹⁹

A unique feature of this study over case-control and cohort studies is the comparison between affected sister pairs in contrast to comparison between affected and unaffected participants.

Selection of unaffected controls in studies of the pathogenesis of UL is especially problematic because UL are very common and often asymptomatic. Although diagnostic ultrasound could be considered to address the disease status of controls, it is financially limiting for large study populations and insensitive to the detection of microscopic tumors. Another distinguishing aspect of this study is the inclusion of women diagnosed by both surgical and non-surgical methods, obviating the possibility of selecting for clinical and demographic characteristics found differentially in hysterectomy-based populations. Also of note, black and white participants in this study had similar educational levels, decreasing the likelihood and magnitude of confounding due to differences in socioeconomic status.

One limitation of this study is that exposures and outcomes are primarily measured through self report. However, diagnosis of UL was confirmed by medical records in 91% of our study participants. Among the 9% of remaining study participants, confirmation of UL diagnosis was often precluded because medical records were not available, likely due to a practice of destroying hospital patient records after seven years. Self-reported UL diagnosis in this study population appears to be relatively accurate. Only three participants (0.6%) who self reported a diagnosis of UL were excluded from analysis because medical records were inconsistent. Participants lacking medical record confirmation were not significantly different with respect to race from participants with medical record confirmation, making differential misclassification of outcome in our regression analyses unlikely. Moreover, regression results did not change when women without medical record confirmation were excluded from the analyses. Underreporting of weight may have occurred, but is unlikely to have changed our findings. Although black women have been shown to underreport their weight by an average of four pounds more than the amount underreported by white women (7.1 versus 3.0 pounds), the difference between self-reported and true weight was small for both groups and rarely resulted in a change in BMI category.²⁰ Moreover, it has been suggested that socioeconomic status is a more powerful determinant than race in weight self-reporting, and our population is of comparable socioeconomic status.²¹ Finally, although we addressed the major confounders of UL presentation in these analyses, additional unidentified confounders may exist that could further clarify factors that influence the severity of UL. Other limitations stem from our current understanding of the natural history of UL. Specifically, UL are a complex genetic disease with various environmental influences that undoubtedly impacts clinical phenotype.

Slight differences between our study population demographics and population-based estimates may impact generalizability of inferences based on this study population. Both black and white participants in our study had a higher rate of OCP use than that reported for women in the U.S. (23% of black women in the U.S. versus 65% in our study and 35% of white women in the U.S. versus 73% in our study), possibly reflecting the ability for participants in our study to access health care resources.²² The generally younger age at diagnosis in our population compared to other reported UL populations might reflect the selection of women with a positive family history and possibly with underlying susceptibility gene(s).^{15, 16} A relatively lower rate of severe pain in our population may result from comparing our data with a hysterectomy-based population that may have had more severe symptoms than our sister pairs who more often underwent non-surgical management.¹⁶

Our finding of a significantly different presentation of disease among black and white women with a family history of UL raises the intriguing and testable question as to whether white and black women with a family history of UL have different underlying genetic liabilities to develop UL. In fact, differences in protein expression in UL from black women and white women have been reported recently by microarray analysis.²³ It is not yet known whether these expression differences also are found in a population of women with a family history of UL. Preliminary studies suggest that further linkage and association studies of our affected sister-pair study population will provide an opportunity to identify UL susceptibility genes likely to vary across

racial groups, such as that we have already observed for fumarate hydratase.²⁴ Incorporating the epidemiologic data described herein with future identification of genetic variants conferring risk or protection will provide greater understanding of UL disease, potentially enabling subsets of women at risk for UL, both across and within racial groups, to tailor treatment and prevention strategies.²⁵

Acknowledgements

Special thanks to Matthew Huyck and Allison Vitronis for their expert help with data management and to our past interns and volunteers: Katherine Ariemma, Marylyn Burrige, Carrie Daniel, Sarah Juhlin, Teka Harris, Purnima Kambli, Kate Kiszewski, Melissa Lobel, Amy Mepani, Melissa Morales, Najila Nassery, Nikki Rouille, Marina Seliverstova, Erin Smith, Sandra Tseng, Benedikt Vandenberg, Michelle Wilson, Cindy Wu, and Jennifer Yeh.

This work was supported by HD046226 (CCM) and an HHMI Predoctoral Fellowship in the Biological Sciences (KLH).

References

1. STEWART EA. Uterine fibroids. *Lancet* 2001;357:293–8. [PubMed: 11214143]
2. KESHAVARZ H, HILLIS SD, KIEKE BA, MARCHBANKS PA. Hysterectomy Surveillance-United States, 1994–1999. *MMWR Surveillance Summaries* 2002;51:1–8.
3. HARTMANN KE, BIRNBAUM H, BEN-HAMADI R, et al. Annual costs associated with diagnosis of uterine leiomyomata. *Obstet Gynecol* 2006;108:930–7. [PubMed: 17012456]
4. FLYNN M, JAMISON M, DATTA S, MYERS E. Health care resource use for uterine fibroid tumors in the United States. *Am J Obstet Gynecol* 2006;195:955–64. [PubMed: 16723104]
5. TRELOAR SA, MARTIN NG, DENNERSTEIN L, RAPHAEL B, HEATH AC. Pathways to hysterectomy: insights from longitudinal twin research. *American Journal of Obstetrics and Gynecology* 1992;167:82–88. [PubMed: 1442963]
6. LUOTO R, KAPRIO J, RUTANEN EM, TAIPALE P, PEROLA M, KOSKENVUO M. Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study. *Maturitas* 2000;37:15–26. [PubMed: 11099869]
7. KURBANOVA M, KOROLEVA AG, SERGEEV AS. Genetic-epidemiological analysis of uterine myoma: estimate of risk to relatives. *Genetika* 1989;20:1896–1898. [PubMed: 2620816]
8. VIKHLYAEVA EM, KHODZHAIEVA ZS, FANTSCHENKO ND. Familial predisposition to uterine leiomyomas. *International Journal of Gynaecology and Obstetrics* 1995;51:127–131. [PubMed: 8635633]
9. ALAM NA, ROWAN AJ, WORTHAM NC, et al. Genetic and functional analyses of FH mutations in multiple cutaneous and uterine leiomyomatosis, hereditary leiomyomatosis and renal cancer, and fumarate hydratase deficiency. *Hum Mol Genet* 2003;12:1241–52. [PubMed: 12761039]
10. TOMLINSON IP, ALAM NA, ROWAN AJ, et al. Germline mutations in FH predispose to dominantly inherited uterine fibroids, skin leiomyomata and papillary renal cell cancer. *Nat Genet* 2002;30:406–10. [PubMed: 11865300]
11. GROSS KL, MORTON CC. Genetics and the development of fibroids. *Clin Obstet Gynecol* 2001;44:335–49. [PubMed: 11344997]
12. SCHWARTZ SM, MARSHALL LM, BAIRD DD. Epidemiologic contributions to understanding the etiology of uterine leiomyomata. *Environ Health Perspect* 2000;108(Suppl 5):821–7. [PubMed: 11035989]
13. FLAKE GP, ANDERSEN J, DIXON D. Etiology and pathogenesis of uterine leiomyomas: a review. *Environ Health Perspect* 2003;111:1037–54. [PubMed: 12826476]
14. PAYSON M, LEPPERT P, SEGARS J. Epidemiology of myomas. *Obstet Gynecol Clin North Am* 2006;33:1–11. [PubMed: 16504803]
15. MARSHALL LM, SPIEGELMAN D, BARBIERI RL, et al. Variation in the incidence of uterine leiomyomata among premenopausal women by age and race. *Obstetrics and Gynecology* 1997;90:967–973. [PubMed: 9397113]

16. KJERULFF KH, LANGENBERG P, SEIDMAN JD, STOLLEY PD, GUZINSKI GM. Uterine leiomyomas: racial differences in severity, symptoms and age at diagnosis. *Journal of Reproductive Medicine* 1996;41:483–490. [PubMed: 8829060]
17. CHANDRA, AMG.; MOSHER, WD.; ABMA, JC.; JONES, J. Fertility, family planning, and reproductive health of U.S. women: Data from the 2002 national survey of family growth. *National Center for Health Statistics; Vital and Health Statistics*: 2005. p. 23
18. LETHBRIDGE-CEJKU, MRD.; VICKERIE, J. *National Center for Health Statistics Vital and Health Statistics*. 10. 2006. Summary health statistics for U.S. adults: National Health Interview Survey, 2004.
19. FACT, SHEET. Adult cigarette smoking in the United States: Current estimates. *National Center for Chronic Disease Prevention and Health Promotion*; 2005.
20. BRUNNER HUBER LR. Validity of Self-reported Height and Weight in Women of Reproductive Age. *Matern Child Health J* 2006
21. CALDWELL MB, BROWNELL KD, WILFLEY DE. Relationship of weight, body dissatisfaction, and self-esteem in African American and white female dieters. *Int J Eat Disord* 1997;22:127–30. [PubMed: 9261649]
22. *Health, United States, 2005 with Chartbook on Trends in the Health of Americans*. Hyattsville, Maryland: *National Center for Health Statistics*; 2005.
23. WEI JJ, CHIRIBOGA L, ARSLAN AA, MELAMED J, YEE H, MITTAL K. Ethnic differences in expression of the dysregulated proteins in uterine leiomyomata. *Hum Reprod* 2006;21:57–67. [PubMed: 16172143]
24. GROSS KL, PANHUUSEN CI, KLEINMAN MS, et al. Involvement of fumarate hydratase in nonsyndromic uterine leiomyomas: genetic linkage analysis and FISH studies. *Genes Chromosomes Cancer* 2004;41:183–90. [PubMed: 15334541]
25. LOBEL MK, SOMASUNDARAM P, MORTON CC. The genetic heterogeneity of uterine leiomyomata. *Obstet Gynecol Clin North Am* 2006;33:13–39. [PubMed: 16504804]

Figure 1.
Severity algorithm

Table 1
 Characteristics of the study population and risk factors for UL among all participants by race

Characteristic	Black (n = 146)	White (n = 424)	p-value
Age (years)			
Mean	40.8 ± 6.1	45.1 ± 8.1	< 0.001
Education Level			
Less than college	30 (20.8)	70 (16.5)	0.51
College graduate	64 (44.4)	198 (46.8)	
More than college	50 (34.7)	155 (36.6)	
Age of Menarche (years)			
Less than 10	13 (9.0)	8 (1.9)	<0.001
10 to 11	41 (28.3)	94 (22.2)	
12 to 13	68 (46.9)	258 (60.8)	
14 to 15	20 (13.8)	55 (13)	
Greater than 15	3 (2.1)	9 (2.1)	
Median	12 [11, 13]	12 [12, 13]	0.01
Currently Menopausal (natural)			
Yes	4 (2.7)	45 (10.7)	0.002
No	142 (97.3)	377 (89.3)	
History of Pregnancy			
Yes	88 (62.0)	295 (70.0)	0.08
No	54 (38.0)	127 (30.0)	
History of Oral Contraceptive Use			
Yes	94 (64.8)	307 (73.1)	0.06
No	51 (35.2)	113 (26.9)	
Current BMI			
BMI < 18.5 (Underweight)	1 (0.7)	7 (1.7)	< 0.001
18.5 ≤ BMI < 25 (Normal Weight)	54 (39.4)	230 (55.2)	
25 ≤ BMI < 30 (Overweight)	33 (24.1)	109 (26.1)	
BMI ≥ 30 (Obese)	49 (35.8)	71 (17.0)	
Weight gain since age 18 compared to current weight (pounds)			
Median	40 [20, 50]	20 [10, 40]	< 0.001
History of Cigarette Smoking			
Current	13 (9.03)	24 (5.7)	0.004
Former	24 (16.7)	128 (30.4)	
Never	107 (74.3)	269 (63.9)	
Exercise Vigorously			
Yes	74 (50.7)	245 (58.1)	0.12
No	72 (49.3)	177 (41.9)	
Hours per Week of Exercise			
≤ 3	32 (43.2)	70 (28.9)	0.02
> 3	42 (56.8)	172 (71.1)	
Age When Began Exercising (years)			
Median	22.5 [16.5, 31.5]	27 [18, 35.5]	0.09

* All data are shown as number (%), mean ± standard deviation (%) or median with [25, 75] percentile ranges

Table 2

Dietary factors among all participants by race

Characteristic	Black (n = 146)	White (n = 424)	p-value
Meat Consumption			
Never	17 (12.7)	34 (8.6)	0.001
Rarely	25 (18.7)	35 (8.8)	
Monthly	29 (21.6)	66 (16.6)	
Weekly	55 (41.0)	237 (59.7)	
Daily	8 (6.0)	25 (6.3)	
Fruit Consumption			
Never	1 (0.7)	0 (0.0)	0.002
Rarely	7 (5.2)	13 (3.3)	
Monthly	9 (6.7)	7 (1.8)	
Weekly	36 (26.9)	81 (20.3)	
Daily	81 (60.4)	298 (74.7)	
Vegetable Consumption			
Never	0 (0.0)	0 (0.0)	0.008
Rarely	3 (2.3)	4 (1.0)	
Monthly	4 (3.0)	6 (1.5)	
Weekly	29 (21.8)	48 (12.0)	
Daily	97 (72.9)	341 (85.5)	
Milk Consumption			
Never	14 (9.9)	27 (6.5)	< 0.001
Rarely	44 (31.2)	49 (11.9)	
Monthly	18 (12.8)	27 (6.5)	
Weekly	38 (27.0)	87 (21.1)	
Daily	27 (19.1)	223 (54.0)	
Coffee Consumption			
Never	56 (38.6)	133 (31.9)	0.01
Rarely	25 (17.2)	44 (10.6)	
Monthly	7 (4.8)	11 (2.6)	
Weekly	11 (7.6)	32 (7.7)	
Daily	46 (31.7)	197 (47.2)	
Tea Consumption			
Never	17 (12.0)	75 (18.3)	0.005
Rarely	37 (26.1)	95 (23.2)	
Monthly	22 (15.5)	43 (10.5)	
Weekly	40 (28.2)	76 (18.5)	
Daily	26 (18.3)	121 (29.5)	
Chocolate Consumption			
Never	6 (4.5)	17 (4.3)	0.004
Rarely	38 (28.8)	67 (16.8)	
Monthly	34 (25.8)	81 (20.3)	
Weekly	40 (30.3)	188 (47.0)	
Daily	14 (10.6)	47 (11.8)	
Red Wine Consumption			
Never	59 (41.5)	139 (34.6)	0.008
Rarely	47 (33.1)	99 (24.6)	
Monthly	19 (13.4)	65 (16.2)	
Weekly	14 (9.9)	70 (17.4)	
Daily	3 (2.1)	29 (7.2)	
Liquor Consumption			
Never	72 (51.1)	155 (38.6)	0.001
Rarely	35 (24.8)	170 (42.3)	
Monthly	21 (14.9)	33 (8.2)	
Weekly	10 (7.1)	36 (9.0)	
Daily	3 (2.1)	8 (2.0)	
Beer Consumption			
Never	85 (59.9)	187 (46.3)	0.02
Rarely	27 (19.0)	119 (29.5)	
Monthly	15 (10.6)	43 (10.6)	
Weekly	11 (7.7)	49 (12.1)	
Daily	4 (2.8)	6 (1.5)	
Alcohol Consumption			
Yes	102 (70.8)	337 (79.9)	0.03
No	42 (29.2)	85 (20.1)	

* All data are shown as number (%)

Table 3
 Characteristics of UL among all participants by race

Characteristic	Black (n =146)	White (n = 424)	p-value
Age of UL Diagnosis (years)	31 [27, 36]	37 [31,42]	< 0.001
Median			
Medical Record Confirmation of UL Diagnosis			0.09
Surgery, UAE, path report	64 (44.1)	173 (40.8)	
Radiological imaging	54 (37.2)	201 (47.4)	
Physical exam, history	8 (5.5)	16 (3.8)	
Records not available	19 (13.1)	34 (8.0)	
Menstrual Cycles Predictable Within 10 Days			0.69
Yes	130 (90.9)	377 (89.8)	
No	13 (9.1)	43 (10.2)	
Days Between Period			< 0.001
Less than 22	30 (21.4)	37 (8.9)	
22 to 26	27 (19.3)	94 (22.5)	
27 to 29	65 (46.4)	190 (45.5)	
30 to 35	16 (11.4)	87 (20.8)	
Greater than 35	2 (1.4)	10 (2.4)	
Number of Days of Flow			0.002
Less than 5	39 (27.1)	67 (15.8)	
5 to 7	85 (59.0)	316 (74.7)	
Greater than 7	20 (13.9)	40 (9.5)	
Amount of Pain With Periods			<0.001
No pain	14 (9.9)	52 (12.4)	
Mild/Moderate	85 (59.9)	306 (72.7)	
Severe pain	43 (30.3)	63 (15.0)	
Surgery Due to UL			0.99
Yes	65 (44.5)	189 (44.6)	
None reported	81 (55.5)	235 (55.4)	
Has Had a Hysterectomy			0.19
Yes	29 (20.3)	109 (25.7)	
No	114 (79.7)	315 (74.3)	
Time Since UL Diagnosis (years)			0.07
Median	8 [3, 13]	6 [2, 11]	

* All data are shown as number (%) or median with [25, 75] percentile ranges

Table 4

Symptom severity among all participants by race

Characteristic	Black (n = 146)	White (n = 424)	p-value
Symptom severity			
Severe	133 (91.1)	303 (71.5)	<0.001
Non-severe	13 (8.9)	121 (28.5)	

* All data are shown as number (%)

Table 5

Logistic regression analysis of severity of UL symptoms

		Odds Ratio	95% confidence interval	p-value
Model 1 (n = 281)	Predictor	5.53	2.13–14.4	<0.001
	<i>Black race</i> [^]			
Model 2 (n = 280)	Predictor	5.22	1.99–13.7	<0.001
	Confounder	0.78	0.62–0.97	0.02
	<i>Black race</i> [^]			
Model 3 (n = 252)	Predictor	5.30	1.92–14.7	0.001
	Confounders	0.75	0.59–0.95	0.017
	Age at menarche [^]	1.63	0.85–3.11	0.14
	No history of pregnancy [^]	1.27	0.68–2.38	0.45
	BMI [≥] 25 [^]	0.58	0.31–1.08	0.09
	Frequent red meat intake [^]	0.93	0.43–2.00	0.84
	Current alcohol use [^]	1.08	0.57–2.04	0.81
	History of cigarette use [^]	0.94	0.50–1.78	0.85
	Oral contraceptive use [^]			

Table 6

Linear regression analysis of age at diagnosis of UL

	Predictor	<i>Black race</i> [^]	β	Standard Error	p-value
Model 1 (n=271)			-6.00	1.12	<0.001
Model 2 (n=267)	Predictor	<i>Black race</i> [^]	-5.33	1.13	<0.001
	Confounders	Age at menarche [^] No history of pregnancy [^]	0.90 -3.03	0.34 0.97	0.009 0.002
Model 3 (n=243)	Predictor	<i>Black race</i> [^]	-5.62	1.26	<0.001
	Confounders	Age at menarche [^]	1.00	0.37	0.007
		No history of pregnancy [^]	-3.19	1.06	0.003
		BMI ≥ 25 [^]	-1.14	1.06	0.28
		Frequent red meat intake [^]	0.97	1.05	0.36
		Current alcohol use [^]	0.85	1.26	0.50
		History of cigarette use [^] Oral contraceptive use [^]	-1.75 1.53	1.09 1.08	0.11 0.16

[^] Black race: dichotomous parameter (yes or no)

Age at menarche: continuous parameter (in years)

History of pregnancy: dichotomous parameter (yes or no)

BMI: dichotomous parameter (low/normal (BMI<25) vs. overweight/obese (BMI ≥ 25))

Red meat intake at least weekly: dichotomous parameter (yes or no)

Current alcohol use: dichotomous parameter (yes or no)

History of cigarette use: dichotomous parameter (yes or no)

Oral contraceptive use before age 20: dichotomous parameter (yes or no)