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Prevalence of Uterine Leiomyomas in the First Trimester of Pregnancy: An Ultrasound Screening Study

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Abstract

Objective—To estimate the proportion of pregnant women with one or more leiomyoma detected by research quality ultrasound screening in the first trimester; to describe the size and location of leiomyomas identified; and to report variation in prevalence by race/ethnicity.

Methods—Within an ongoing prospective cohort we conducted 4,271 first trimester, or post-miscarriage, ultrasounds. Sonographers measured each leiomyoma three separate times, recording the maximum diameter in three perpendicular planes each time. Sonographers and investigators classified type and location.

Results—Among 458 women with one or more leiomyomas (prevalence 10.7%), we identified a total of 687 leiomyomas. The mean size of the largest leiomyoma was 2.3cm (95% CI 1.8 to 2.8). Mean gestational age at ultrasound was 61 ± 13 days from last menstrual period. Prevalence varied by race/ethnicity: 18% in blacks (95%CI: 13, 25); 8% in whites (95%CI: 7, 11); and 10% in Hispanics (95% CI: 5, 19). The proportion of women with leiomyomas increased with age much more steeply for blacks than whites.

Conclusions—Leiomyomas are common in pregnancy and occur more often among black women. Given the limited research on effects of leiomyomas on reproductive outcomes, the degree to which race/ethnic disparities in prevalence of leiomyomas may contribute to disparities in events like miscarriage and preterm birth warrants investigation.

INTRODUCTION

Uterine leiomyomata are common and concerning. Leiomyomata have been associated with adverse pregnancy outcomes including difficulty conceiving, spontaneous abortion, preterm birth, placental abruption, and cesarean birth (1-8). By age 35 among non-pregnant women, more than 60% of black women and almost 40% of white women have leiomyomata

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identifiable by imaging (9). Thus, overall prevalence in pregnancy could average 10 to 20%, with higher prevalence in women of advancing maternal age. Little is known about either prevalence of leiomyomata or their reproductive risks from prospective studies in pregnant populations that reflect the general population of the United States (10). Available information has been gathered in subgroups such as women seeking care for infertility, from European populations, and from ultrasound databases of academic medical centers (11-15).

Advances in ultrasound have made some prior operational definitions obsolete. The Muram criteria have been widely used in research to define the presence of a leiomyoma by ultrasound. The original criteria included visualization of a spherical mass with diameter ≥ 3cm; distortion of the adjacent myometrium by the mass; and a distinctive echogenicity, differentiating the mass from myometrium (16). Improvements in ultrasound resolution suggest we can now confidently identify and measure smaller leiomyomata. Prior literature reports prevalence of leiomyomata in pregnancy is less than 1% to 5% (8,14,17-20). A low prevalence in these studies may result from 1.) operational definitions requiring a large diameter to define presence of leiomyomata; 2.) inconsistent documentation of leiomyomata in clinical databases subsequently used for research; 3.) difficulty detecting leiomyomata as pregnancy progresses and uterine anatomy, fetus, and placenta interfere with complete assessment of the myometrium; or 4) study populations that are highly selected for younger women.

Using a prospective study design with community-based recruitment and research quality ultrasound for all participants, we sought to: 1.) estimate what proportion of women have leiomyomata ≥0.5cm maximum diameter in the first trimester of pregnancy; 2.) describe the size, type, and location of leiomyomata identified; and 3.) report any variation by race/ethnicity.

Materials and Methods

Right from the Start (RFTS) is a prospective, cohort study of pregnancy that includes women from four metropolitan areas in three states (NC, TN, TX). IRB approval was obtained from each of four participating academic institutions. Women included in this analysis were recruited from 2001 to 2007 using multiple approaches including print materials in community practices, direct home mailings, pregnancy test kit coupons at pharmacies, newsletters and advertisements (21). The study is described in outreach materials as a study of early pregnancy health and has never been advertised as a study about leiomyomata in pregnancy. Women were eligible to participate if they were 18 years or older, enrolled by 12 6/7 weeks gestation based on last menstrual period (LMP), did not use assisted reproductive technology, intended to carry the pregnancy to term, spoke English or Spanish, and did not plan to move for the next 18 months. Women could re-enroll for subsequent pregnancies, but only first enrollments with ultrasound data on leiomyoma status were included in this analysis.

The study was designed to enroll women very early in pregnancy. Women who were planning a pregnancy were “pre-enrolled” for up to six months and were enrolled once they reported a pregnancy (n=858); the balance enrolled in the first trimester. An abbreviated interview was done at intake and a more detailed computer-assisted telephone interview was conducted in the first trimester including extensive reproductive and medical history. Women self-reported race and ethnicity. This interview also gathered information about diagnosis and treatment of leiomyomata prior to the current pregnancy.

Endovaginal ultrasound without Doppler (supplemented if needed by trans-abdominal images), was scheduled for all participants aiming for the beginning of the sixth week of gestation. Beginning in January 2005, participants who reported a pregnancy loss prior to the scheduled ultrasound were also invited to have an ultrasound; this was scheduled within two weeks of their report (n=56). Sonographers at each study site were required to have three or more years of clinical obstetric-gynecologic experience. They received additional research training on uniformity in identifying and measuring leiomyomata and were instructed not to discuss leiomyoma history with participants.

Presence of a leiomyoma was defined by the Muram criteria with modification to include masses of maximum diameter ≥0.5cm (16). When a leiomyoma was identified, the diameter was measured in three perpendicular planes. During the ultrasound, sonographers returned twice more to each leiomyoma to record the same measurements. (Intervening time was used to record gestational structures). Triplicate measures were intended to reduce the chance that focal contractions would be misclassified as leiomyomata. Leiomyoma diameters were averaged across all three measures and a mean diameter was calculated for each leiomyoma. We refer to mean diameter of the largest leiomyoma when we use the term leiomyoma size.

Leiomyomata were “mapped” onto a uterine diagram and were categorized by location (fundus, corpus, lower segment), position (anterior, posterior, right and left), and type. Type was defined in mutually exclusive categories: submucous – any leiomyoma in contact with or distorting the uterine cavity without identifiable myometrium between the leiomyoma and the endometrium; subserous – distorting the external contour of the uterus; intramural – within the myometrium, neither distorting contour nor cavity; and pedunculated – attached to the uterus with an identifiable stalk. Women with multiple leiomyomata had each leiomyoma documented separately. Leiomyoma and fetal images were saved initially in still, print images, and later as digital images on CD-ROM and sent to the study office for review by study investigators.

For analyses describing prevalence of leiomyomata, we adjusted for correlation within the three study sites (North Carolina, Tennessee, and Texas) using generalized estimating equations (22,23). For analyses of fibroid size we used the logarithm of the diameter for normalization, and the geometric means are reported. Mixed models (24) were used to adjust for correlations within study site when describing fibroid size among women with fibroids present. Age-related changes in leiomyoma prevalence, multiplicity, and size were not examined for Hispanics because of limited numbers. The χ^2 test was used for comparing categorical data on leiomyomata (type, location, and position) by ethnicity. We used two-sided significance testing and considered $p<0.05$ statistically significant in presentation of results. Data were analyzed with SAS 9.1 (SAS Institute, Cary, N.C.) and STATA10.0 (Stata Corporation, College Station, TX).

RESULTS

We enrolled 4,582 women of whom 4,271 had ultrasounds and were enrolled for the first time (Table 1). Women who did not complete an ultrasound (n=311) were similar to those who did in terms of maternal age, race/ethnicity, parity, marital status and education level. Ultrasounds were completed an average of 61 days ±13 days from self-reported LMP. Leiomyoma prevalence did not differ by gestational age at ultrasound (p=0.3).

The prevalence of one or more leiomyomata was 10.7% (95% confidence interval (CI): 8.5, 13.6). Among 458 women with one or more leiomyomata, we identified a total of 687 leiomyomata. Maximum leiomyoma diameter ranged from 0.5cm to 12.9cm. The mean size of the women’s largest leiomyoma was 2.3cm (95% CI 1.8 to 2.8cm). Subserosal (42%) and intramural (35%) leiomyomata were most common; 17% were submucous, and 5% were

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pedunculated. Nearly half of all leiomyomata occurred in the uterine corpus and 35% were in the fundus. Leiomyomata were evenly distributed in anterior and posterior as well as on the right and left sides of the uterus (p=0.2). Leiomyoma type and location did not differ between blacks and whites (p≥0.1 for each comparison) except that black women had slightly more leiomyomata in the posterior wall of the uterus than white women (p=0.03). Seventy-two percent of women with a leiomyoma did not report a diagnosis of leiomyomata prior to this pregnancy.

Although overall leiomyoma prevalence was 10.7%, prevalence differed by race/ethnicity. Black women (n=915) had a prevalence of 18% (95% CI: 13, 25); white women (n= 2,826), 8% (95% CI: 7, 11); Hispanic women (n=335), 10% (95% CI: 5, 19); and the "other" group, predominantly Asian (n=186), 13% (95% CI: 10, 16). Leiomyomata were present in women as young as 19 years old. For black and white women we had sufficient numbers of participants to examine differences with age. Prevalence among those under 25 years old was 6% (95% CI: 3, 10) in black women and 4% (95%CI: 3, 7) in whites. Prevalence increased with age for both blacks and whites (Figure 1). The rise in prevalence by age was steeper among black women (p=0.02).

Among those with leiomyomata, having two or more leiomyomata also differed by race/ ethnicity: 39% of black women with leiomyomata had multiple tumors (95% CI: 37, 42), 20% of white women (95% CI: 20, 21), and 22% of Hispanic women (95% CI: 11, 42). The presence of multiple tumors increased with age for black women from 22% (95% CI: 14, 35) for women younger than 30, to 58% (CI 52, 65) for women 35 years and older. For white women, the proportion with multiple tumors increased slightly across age from 19% (95% CI: 16, 22) in women younger than 30 to 25% (95% CI: 22, 29) for women 35 years and older (Figure 2). This difference in the proportion of women with multiple tumors as age advances was significantly different between blacks and whites (p=0.005).

Average size of the women's largest leiomyoma differed by race/ethnicity as well. Average size was 2.5cm (95% CI: 2.1, 3.1) for black women. This was not different from the average leiomyoma size for Hispanics, 2.4cm, (95% CI: 1.8, 3.1), but significantly larger than average leiomyoma size for white women, 2.0cm, (95% CI: 1.6, 2.4, p=0.0002). Leiomyoma size tended to be larger in older compared with younger black women, but there was little variation in size with age for whites. However, the difference between blacks and whites was not statistically significant (p=0.08).

Prevalence estimates are intrinsically determined by the operational definition of the size of a leiomyoma required to classify a mass as a leiomyoma. If we were to define prevalence based on the original Muram criteria restricting leiomyoma diameter to ≥3.0cm, prevalence is 7% in black (95% CI: 5, 10) and 3% in white women (95% CI: 2, 3), p<0.001. Another common cut-point, requiring a diameter of ≥1.0cm, results in prevalence of 16% in black (95% CI: 12, 22) and 7% in white women (95%CI: 6, 9), p<0.001.

DISCUSSION

We have estimated the prevalence of leiomyomata in pregnancy by uniformly screening women during the first trimester. Our findings indicate a higher prevalence than previously reported. These higher estimates are more compatible with those required to reach the prevalence documented in imaging studies of older, non-pregnant women. We have confirmed that leiomyomata are common and occur with increasing frequency with advancing age.

Our data on race/ethnicity, in a younger population than those previously screened for leiomyomata, are consistent with prior reports. We found that black women are more likely to have leiomyomata and to have more numerous and larger leiomyomata. Hispanic women appeared to have leiomyoma characteristics similar to those of white women; however, screening of larger groups of Hispanic women will be required.

The majority of our participants were unaware of their leiomyoma status prior to the study ultrasound. Thus, we do not believe the sample was biased by a predominance of women with leiomyomata seeking participation. However, due to the nature of this cohort with predominantly planned pregnancies, we were not surprised that the participants were older, more educated, less likely to smoke and more likely to be married than the general population (25). Because our participants were pregnant, our cohort is limited to fertile women. Leiomyomata may be associated with impaired fertility (7). If so, our findings would underestimate the true prevalence in this age group. Leiomyomata might also be related to pregnancy loss. If so, this too will result in an underestimate of tumor prevalence because those with a loss prior to their scheduled ultrasound were invited to have ultrasounds only in the last few years of data collection and those invited were less likely to keep post-loss ultrasound appointments than their pregnant counterparts. The current dataset includes only 56 of these women.

In 1970, the median age of women who gave birth in the United States was 25.4; in 2000 it was 27.1 (26). This shift in the demographics of maternity makes a more nuanced understanding of leiomyomata in pregnancy of increasing importance because larger proportions of women and their pregnancies are affected. We lack knowledge about the precise relationship of leiomyomata to adverse pregnancy outcomes and the risks and benefits of leiomyoma intervention in reproductive women (10). Additionally, black women experience a disproportionate share of pregnancy complications; and potentially as a result of the higher prevalence and larger leiomyomata, they also have increased likelihood of surgical interventions for leiomyomata. To provide the best informed care, the research community must continue to pursue an understanding of the degree to which racial and ethnic differences in prevalence of leiomyomata contribute to disparities in events like miscarriage and prematurity. If leiomyomata do increase adverse pregnancy outcomes, determining which interventions to use in the treatment of leiomyomata may reduce poor outcomes and help mitigate disparities.

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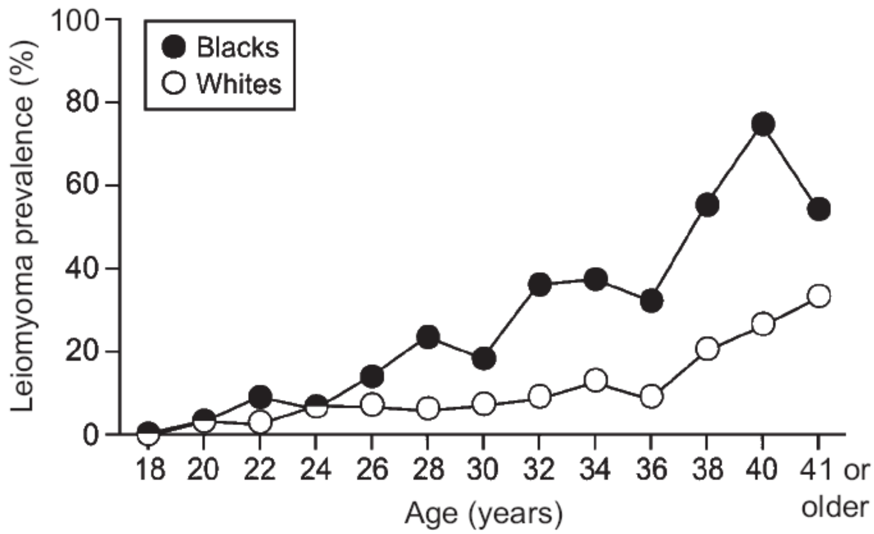

Figure 1. Prevalence of Uterine Leiomyomas among Black (n=915) and White Women (n=2826)*†

*Prevalence is for 2-year age intervals (18= 17 and 18 year olds, 20= 19 and 20 year olds, etc).

†Sample size was too small for evaluation of prevalence by age in other race/ethnic categories because there were fewer than five participants per cell in some cells.

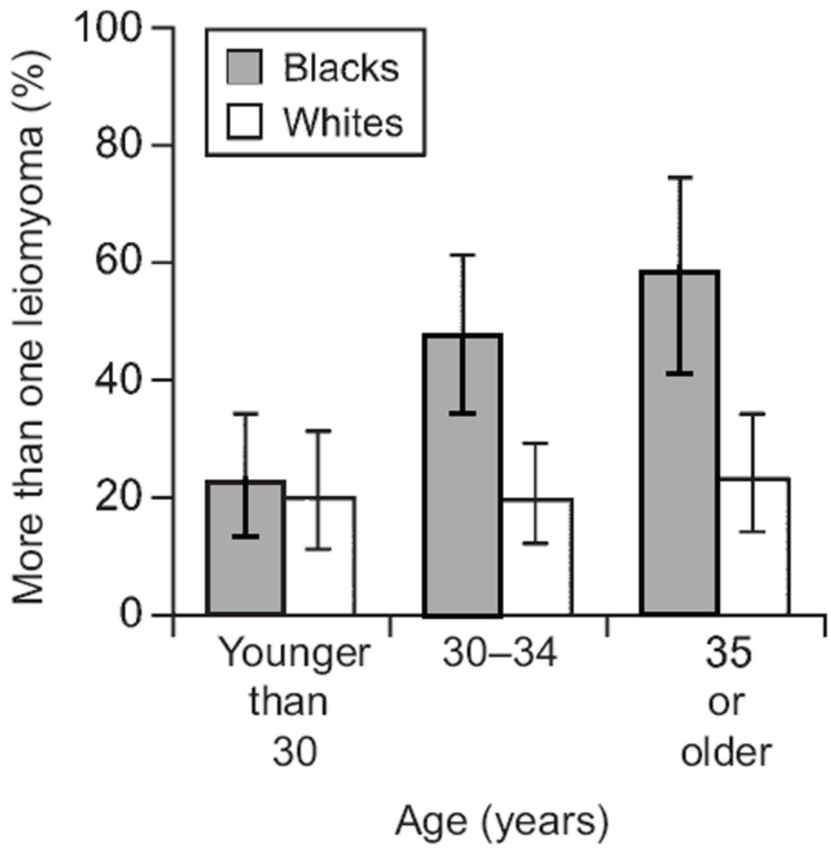

Figure 2. Percentage of Women with More Than One Leiomyoma among Those with Leiomyomas

†Sample size was too small for evaluation of prevalence by age in other race/ethnic categories because there were fewer than five participants per cell in some cells.

Table 1

Characteristics of First Trimester Cohort Screened by Ultrasound for Uterine Leiomyomas

	Black†	White	Hispanic‡
N	915 (21%)	2826 (66%)	335 (8%)
Mean age	26.1 (SD 5.6)	29.8 (SD 4.8)	27.0 (SD 5.5)
Age groups	n (%)	n (%)	n (%)
17-24	423 (46)	360 (13)	124 (37)
25-29	243 (27)	993 (35)	108 (32)
30-34	169 (18)	1007 (36)	67 (20)
≥35	80 (9)	466 (17)	34 (10)
Missing			2
Parity			
0	379 (45)	1293 (48)	130 (42)
1	253 (30)	992 (37)	107 (35)
2+	208 (25)	425 (16)	69 (23)
Missing§	75	116	29
BMI			
Underweight(<20)	58 (6)	303 (11)	20 (7)
Normal weight (20-24.9)	238 (27)	1465 (52)	122 (40)
Overweight (25-29.9)	253 (28)	620 (22)	87 (29)
Obese (≥30)	344 (39)	407 (15)	73 (24)
Missing	22	31	33
Education			
High school	375 (41)	311 (11)	159 (47)
Some college	267 (29)	432 (15)	75 (22)
≥4 years of college	273 (30)	2082 (74)	101 (30)
Missing	0	1	0
Marital Status			
Married/co-habiting	574 (63)	2672 (95)	285 (85)
Other	341 (37)	154 (5)	50 (15)
Smoking			
Never	686 (78)	1906 (70)	249 (79)
Past	148 (17)	696 (26)	59 (19)
Current	43 (5)	117 (4)	8 (3)
Missing‡	38	107	19

*Ethnicity other than black, white or Hispanic included Asian, Native American, and other (n=190).

†p<0.001 for all comparisons of black and white women.

‡p<0.01 for comparisons of Hispanic and white women; p<0.05 for comparisons of Hispanic and black women except for parity and smoking (non-significant).

§The majority of missing data include women who completed the early pregnancy ultrasound but not the first trimester interview (n=161).