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Self-Reported Reproductive Tract Infections and Ultrasound Diagnosed Uterine Fibroids in African-American Women

Kristen R. Moore, MSPH,[1,2] Stephen R. Cole, PhD,[1] Dirk P. Dittmer, PhD,[3] Victor J. Schoenbach, PhD,[1] Jennifer S. Smith, PhD,[1] and Donna D. Baird, PhD[2]

Abstract

Background: For decades, it has been hypothesized that reproductive tract infections (RTIs) are risk factors for uterine fibroids. However, only two recent studies have been conducted. We aimed to investigate the relationship between RTIs and fibroids in a large study using ultrasound screening for fibroids.
Methods: We used cross-sectional enrollment data from African American women ages 23–34 years with no previous fibroid diagnosis. RTI history was measured by self-report and fibroid status by standardized ultrasound. Secondary fibroid outcomes were size, number, and total volume. Age- and multivariable-adjusted logistic regression were used to estimate odds ratios (ORs).
Results: In total, 1,656 women were included; 22% had fibroids. Bacterial vaginosis (BV) was associated with a 21% increased odds of fibroids [aOR 1.21, 95% confidence interval (CI) 0.93–1.58]. Chlamydia infection and pelvic inflammatory disease were associated with a 38% (aOR 0.62, 95% CI 0.40–0.97) and a 46% (aOR 0.54, 95% CI 0.25–1.17) reduced odds of having two or more fibroids, respectively. Those with a previous BV diagnosis had a 47% increased odds of having 2 or more fibroids (aOR 1.47, 95% CI 0.98–2.21) and a 41% increased odds of having a larger total fibroid volume (aOR 1.41, 95% CI 0.98–2.04).
Conclusions: Our study was the first to explore the relationship between RTIs and fibroid size, number, and total volume. There appeared to be no strong associations between self-reported RTIs and fibroids. Studies using serology, a biochemical measure of past infection, are needed to better investigate associations between RTIs and fibroids.

Introduction

Uterine fibroids, benign, smooth-muscle-cell tumors of the uterus, are one of the most common gynecologic conditions affecting women during their reproductive years.[1] By age 50 years, the estimated risk of developing fibroids is >80% for African American women and close to 70% for white women.[2] The majority of women with fibroids are asymptomatic; however, an estimated 20%–50% of women experience symptoms (i.e., pelvic pain and pressure, severe bleeding, and reproductive problems).[1,3–5] The primary treatment for fibroids is hysterectomy, and they are the leading indication in the United States, accounting for 40% of all procedures. The total estimated costs of fibroids in the U.S. are as much as $34 billion annually.[6]

Although fibroids are responsible for substantial morbidity and public health burden, their pathogenesis and etiology are largely unknown. Fibroids are hormonally responsive;[7] they develop after menarche[8] and tend to regress after menopause.[9] However, what causes the initial transformation of muscle cells into abnormal muscle cells and then their proliferation and growth into clinically visible tumors is not understood.

Risk factors that have been established for fibroids are African American heritage (African Americans are two to three times as likely to have clinically recognized fibroids as white women),[6] older age (up to the age of menopause), younger age at menarche, and nulliparity.[10–13] Other factors such as body mass index (BMI), smoking, and hormonal contraceptive use have been inconsistently associated with fibroid risk.[10,14,15] More recent studies have shown no association with fibroids and smoking.[15] Two studies have reported that progestin-only injectables (i.e., Depo-Provera) may be protective.[11,16] Alcohol use may be a risk factor, but the number of studies is small.[15,17]

[1]Departments of Epidemiology, Gillings School of Global Public Health, and [3]Microbiology and Immunology, Program in Global Oncology at the Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
[2]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina.

In the 1930s, Witherspoon[18] hypothesized that reproductive tract infections (RTIs) play an etiological role in fibroid development. Both RTIs and fibroids disproportionately burden African American women and certain RTIs can lead to conditions (i.e., chronic pelvic infection) that could result in inflammatory reactions. Rates of reportable RTIs (i.e., chlamydia and gonorrhea) are 6 and 14 times as high among African American women compared with white women, respectively.[19] In addition, rates of chlamydia and gonorrhea are highest among younger women ages 15–24 years which is, in most cases, the period before the diagnosis of fibroids.[20] This hypothesis is consistent with another theorized mechanism of fibroid pathogenesis involving tissue damage and aberrant tissue repair/regeneration (increased extracellular matrix, cell proliferation, and decreased apoptosis), leading to the formation and growth of uterine fibroids.[21,22]

Yet, very few studies have investigated the effect of RTIs on fibroid development. The two recently published studies have only partially consistent results.[10,23] The first was a clinic-based case-control study of fibroid risk factors in the Baltimore metropolitan area with fibroids confirmed by histology or ultrasound.[23] A positive dose–response association was observed between the number of self-reported pelvic inflammatory disease (PID) episodes and uterine fibroids. No association was found between self-reported history of genital herpes or warts and fibroids, although there was a suggestion of an increased odds of fibroids for women with self-reported history of chlamydia.[23]

The Uterine Fibroid Study (UFS)[10] was a cross-sectional study of randomly selected members of an urban health plan screened for fibroids with ultrasound. No association of fibroids was found with self-reported diagnosis of PID. However, there were suggestions of positive associations with self-reported history of chlamydia in white women, and with trichomonas, syphilis, and ''other infections'' (mainly bacterial vaginosis [BV]) in African American women. Self-reported history of genital herpes had nonsignificant elevated odds ratios (ORs) in both ethnic groups.[10] In both studies,[10,23] self-reported history of abnormal Pap smear was inversely associated with fibroids. This finding was also corroborated in our recent study that showed an inverse association between self-reported cervical treatment and fibroids.[24]

A small study of 20 UFS participants examined fibroid tissue for evidence of herpes simplex virus 1 and 2; cytomegalovirus; human herpesvirus 6, 7, and 8; Epstein-Barr virus; and chlamydia[10] using polymerase chain reaction and histology. They did not detect any evidence of these pathogens in the tumor samples.

The goal of this study was to further investigate the relationship between self-reported RTIs and fibroids in a large study of African American women with ultrasound screening for fibroids. We also explored the relationship between self-reported RTIs and number, size, and total volume of fibroids, which has not previously been done.

Materials and Methods

We used transvaginal ultrasound results and self-reported questionnaire data from participants in the ongoing National Institute of Environmental Health Sciences (NIEHS) Study of Environment, Lifestyle, and Fibroids (SELF) based in the Detroit area. We used cross-sectional enrollment data with history of RTIs measured by self-report as the exposures of interest. Fibroid status measured by ultrasound at enrollment was the outcome. Secondary outcomes were size of the largest fibroid, number of fibroids, and total fibroid volume.

Study participants and data collection

SELF is a prospective cohort study of fibroid development. Enrollment and data collection have been described previously.[24] In brief, from November 2010 to December 2012, the study enrolled a volunteer sample of 1,696 African American women ages 23–34 without a prior diagnosis of fibroids in the Detroit, Michigan area. Women were not eligible for SELF if they had previously been diagnosed with uterine fibroids; had a hysterectomy; had ever taken medication to treat lupus, Grave's disease, Sjogren's scleroderma, or multiple sclerosis; or ever had any type of cancer treated with radiation or chemotherapy.

During 2010–2012, recruitment materials, primarily composed of targeted letters, media announcements, and flyers, were distributed throughout the Detroit area with the aim of informing the target population about the study. Interested volunteers called the study number and began the enrollment process including an orientation that thoroughly described study activities. Those that completed all enrollment questionnaires and a clinic visit with ultrasound were enrolled. Participants gave written informed consent. The study was approved by the institutional review boards of NIEHS and Henry Ford Health System (HFHS), a large medical provider in the Detroit area and a collaborating institution.

Fibroid assessment

Transvaginal ultrasound is the standard procedure for the detection and diagnosis of fibroids.[25] It is as accurate as magnetic resonance imaging for women with no more than four fibroids.[25] Fibroids were assessed by study sonographers as described previously[26] at one of three HFHS clinics. Focal fibroids of 0.5 cm diameter or greater were measured in triplicate. For each measurement, the three perpendicular diameters (longitudinal [L], anterior–posterior [A] and transverse [T]) were recorded.

Outcome definitions

The primary outcome of this study was fibroid presence (yes/no) at the transvaginal ultrasound examination completed at enrollment. Questionable fibroids were those for which at least 1 diameter could not be measured. Participants who had at least one fibroid or questionable fibroid ≥ 0.5 cm at enrollment ultrasound (22%; $n = 377$) were considered to have fibroids, and all women who did not have a fibroid or questionable fibroid ≥ 0.5 cm in diameter at enrollment ultrasound ($n = 1{,}319$) were considered to not have fibroids. The secondary outcomes were size of the largest fibroid, number of fibroids, and total fibroid volume. The size of the largest fibroid was determined by averaging the maximum diameter (L, A, or T) of each of the triplicate fibroid measurements. Fibroid volume (cm^3) was measured by computing the volumes of each of the triplicate fibroid measurements using the ellipsoid formula ($L \times A \times T \times 0.5233$), and averaging across the three volumes. Total fibroid volume (cm^3) was calculated by adding the average volumes from each of a

woman's fibroids. Total fibroid volume was not computed for women with only questionable fibroids (n = 6) because at least 1 diameter was not measured.

Reproductive tract infection assessment

At enrollment, SELF participants responded to questions regarding their history of RTIs via a self-administered computer-assisted web interviewing (CAWI) questionnaire. Each question on the CAWI required an answer before the next question was presented. If no answer was recorded, the same question was presented again, but an additional response category was offered: ''prefer not to answer.''

The questions of interest used for this study were: (1) Has a doctor or other health professional ever told you that you had …? (2) How old were you when you were first diagnosed with …? (3) In total, how many times have you been diagnosed with …? These questions were asked for PID, chlamydia, bacterial vaginosis, gonorrhea, trichomonas, genital herpes, and genital warts.

For each RTI, those exposed were the women who reported ''Yes'' to ever being diagnosed with that particular RTI. The unexposed were those who reported ''No'' to ever being diagnosed with that particular RTI. We also created a variable, ''any RTI,'' representing whether the participant had been diagnosed with any of the aforementioned RTIs. The exposed group included those who self-reported at least one RTI diagnosis, and the unexposed group comprised those who did not self-report any RTI diagnosis. Two participants were not included because they responded ''prefer not to answer'' for at least one RTI and reported ''no'' for other RTIs; thus, we could not determine their ''any RTI'' status.

Statistical analyses

Because the majority of questions were asked via telephone or web-based interview where participants had to respond to a question before proceeding, there was minimal missing data. Any ''prefer not to answer'' response (0.06%–0.12%) was coded as missing, and complete case analysis was performed. Variables were categorized based on the distribution of the data and comparability with the literature. All analyses were completed on women who reported ever being sexually active and who did not self-report a diagnosis of human immunodeficiency virus (HIV) or use of HIV medications. Standard descriptive statistics were performed for all variables of interest. For categorical variables, proportions at each level were described. For continuous variables, medians (interquartile ranges) were computed. Although sexual behavior variables are not confounders, we described the relationship between each RTI and number of sexual partners and age at first intercourse for comparison with the literature. All analyses were conducted with SAS 9.3.

Primary analyses: Association between RTIs and fibroid presence

Logistic regression models were used to compute ORs and 95% confidence intervals (CIs) to evaluate the associations between the self-reported RTI-related variables (PID, chlamydia, gonorrhea, trichomonas, BV, genital herpes, and genital warts) and fibroid presence. Because fibroids are common, the relative odds will overestimate the relative risk, but it provides a valid method of testing for statistically significant differences between those with and without a self-reported RTI diagnosis. Potential confounders were determined based on a review of the literature and a directed acyclic graph and were included in the full model: age in years (continuous); age at menarche (7–10, 11–19 years); parity (nulliparous, parous); education (high school/general education development (GED) or less, some college/associates/technical, bachelors/masters/doctorate); body mass index (BMI) (15–24, 25–29, 30–34, ≥35) in kg/m^2; alcohol (low, moderate, heavy); and use of Depo-Provera (ever, never). The alcohol variable reflected the drinking level each woman reported for the age(s) when she was drinking the most. Low drinkers were those who never had 10 or more drinks in a year. Heavy drinkers were those who usually drank 6 or more drinks on days when they drank or drank 4+ drinks per sitting at least 2–3 times a month. Moderate drinkers were all others.

We evaluated the association of ''any RTI'' and each self-reported RTI with fibroids in both age- and multivariable-adjusted models. To control for confounding of an RTI–fibroid association by another RTI, all RTIs were included in the multivariable-adjusted model together [with the exception of PID, which was modeled separately because it can share causal pathways with other RTIs (e.g., chlamydia can cause PID, so only the proximate factor, PID, would be included in a model investigating effects of PID)]. Spearman partial correlations (adjusted for age) among the other RTIs were assessed to assure they were not highly correlated (Supplementary Table S1; Supplementary Data are available online at www.liebertpub.com/jwh).

Secondary analyses

As a secondary analysis we examined the association between RTIs and three outcomes: size of the largest fibroid, number of fibroids, and total fibroid volume. Medians rounded to the nearest whole number were used to determine category cutpoints for size of the largest fibroid and total fibroid volume (2cm and $2cm^3$, respectively). To estimate the ORs and 95% CIs for the association of ''any RTI'' and each RTI and fibroids, we used multinomial logistic regression with the same potential confounders as in the primary analysis. All RTIs were included in the models together (with the exception of PID, which was modeled separately).

As a secondary analysis to examine the association between RTI exposure severity and fibroid presence, we evaluated age- and multivariable-adjusted ORs of the association between the number of times diagnosed with each RTI and the presence of fibroids using two indicator variables (1 vs. none; 2+ vs. none). Because of limited numbers of women reporting multiple infections, each separate RTI was modeled without adjusting for other RTIs. In addition, we looked at whether self-reporting more than one type of infection increased the odds of fibroids using three indicator variables (1 vs. none; 2 vs. none; 3+ vs. none).

Sensitivity analyses

Syphilis was reported by too few women to analyze separately ($n = 15$), but we repeated the primary analyses after excluding them to make sure they were not influential. Cervical treatment is an indicator of cervical lesions secondary to persistent HPV infection and was found to be inversely

associated with fibroids in our previous study.[24] Thus, the RTI associations we were investigating might be attenuated. Therefore, we repeated the primary analyses after excluding those who reported cervical treatment (n = 229).

Results

Of the 1,696 women enrolled, 40 were excluded (34 reported never having sex and 6 reported having HIV). Seventy percent of participants reported at least one RTI diagnosis (Table 1). Those with a prior history of an RTI, compared with women without one, tended to be older, more educated, heavier drinkers, parous, to have ever used Depo-Provera, to have more sex partners before age 20 years, and to have been younger at first sex (Table 1). The prevalences of specific self-reported RTI diagnoses were: 10% for PID, 38% for chlamydia and BV, 32% for trichomonas, 20% for gonorrhea, 9% for genital herpes, and 7% for genital warts (Supplementary Table S2). The median time since first diagnosis of any RTI was 9 years (interquartile range: 5–13 years) (Supplementary Table S3).

Twenty-two percent (22%) of women had fibroids discovered at ultrasound screening (Table 2). Of those with fibroids, the size of the largest fibroid was < 2 cm for 62%; 63% had only one fibroid. The total fibroid volume was $< 2 cm^3$ for 52% of participants with fibroids.

In primary analyses, age-adjusted and multivariable adjusted estimates were very similar (Table 2). Self-reported BV had a positive association with fibroids though not significant (aOR 1.21, 95% CI 0.93–1.58). In secondary analyses, we examined size of the largest fibroid, number of fibroids and total fibroid volume as the outcomes (Fig. 1). Women who reported any RTI had an elevated odds of a small fibroid (aOR 1.31, 95% CI 0.93–1.84). There was a 38% reduction in the odds of having two or more fibroids for chlamydia (aOR 0.62, 95% CI 0.40–0.97) and a 46% reduction for PID (aOR 0.54, 95% CI 0.25–1.17). Those with a previous diagnosis of BV had a 47% increase in the odds of having two or more fibroids (aOR 1.47, 95% CI 0.98–2.21) and a 41% increase in the odds of having a larger total fibroid volume ($\geq 2 cm^3$) (aOR 1.41, 95% CI 0.98–2.04).

In the secondary analyses that examined ''severity'' of RTI based on number of different RTIs we saw an increase in odds of fibroids for those with two RTIs (aOR 1.41, 95% CI 0.99–2.01), but the odds was not elevated for those with three or more RTIs (Supplementary Table S4). Multiple diagnoses of the same RTI were not associated with higher odds of fibroids (Supplementary Table S4).

The first sensitivity analysis, exclusion of those with a self-reported diagnosis of syphilis ($n = 15$), resulted in little change in associations between RTIs and fibroid presence (data not shown). However, the second sensitivity analysis, removal of those with a self-reported diagnosis of cervical treatment ($n = 229$), resulted in a somewhat stronger association for genital warts (aOR 1.29, 95% CI 0.76–2.18). Other RTI associations were essentially unchanged (data not shown).

Table 1. Distribution of Covariates by Self-Reported Reproductive Tract Infection Status

Covariate	*Any reproductive tract infection*[a] *Yes* (N = *1,172*) n *(%)*	*No* (N = *482*) n *(%)*
Age		
23–26	343 (29)	157 (33)
27–30	396 (34)	170 (35)
≥ 31	433 (37)	155 (32)
Education		
≤ High school/GED	229 (20)	133 (28)
Some college or technical	639 (55)	201 (42)
≥ Bachelors	303 (26)	148 (31)
Missing	1	
BMI (kg/m^2)		
15–24	212 (18)	111 (23)
25–29	266 (23)	78 (16)
30–34	236 (20)	84 (17)
≥ 35	458 (39)	209 (43)
Alcohol at age when drinking the most[b]		
Low	255 (22)	172 (36)
Moderate	386 (33)	157 (33)
Heavy	531 (45)	153 (32)
Parity		
Nulliparous	409 (35)	218 (45)
Parous	763 (65)	264 (55)
Depo-Provera		
Never used	638 (54)	300 (62)
Ever used	534 (46)	182 (38)
Age at menarche (years)		
7–10	206 (18)	96 (20)
11–19	966 (82)	386 (80)
Sex partners before age 20 years		
≤ 1	203 (17)	190 (39)
2–5	588 (50)	237 (49)
≥ 6	379 (32)	55 (11)
Missing	2	
Age at first sex (years)		
≤ 14	407 (35)	83 (17)
15–16	426 (36)	143 (30)
≥ 17	338 (29)	254 (53)
Missing	1	2

Any ''prefer not to answer'' response was coded as missing.

[a]Includes pelvic inflammatory disease, chlamydia, bacterial vaginosis, trichomonas, gonorrhea, genital herpes, and genital warts. Two participants were not included because they responded ''prefer not to answer'' for at least one RTI and reported ''no'' for other RTIs; thus, their ''any RTI'' status could not be determined.

[b]Low drinkers were those who never had 10 or more drinks in a year. Heavy drinkers were those who usually drank 6 or more drinks on days when they drank or drank 4+ drinks per sitting at least 2 to 3 times a month. Moderate drinkers were all others.

BMI, body mass index; GED, general education degree; IQR, interquartile range.

Discussion

In this large study of young African American women, there was little overall support for an association between women's self-reported histories of RTIs and subsequent fibroid development. Even those having a history of three or more different RTIs or multiple diagnoses of the same RTI showed no indication of elevated odds of fibroids. However, our results for BV and chlamydia are suggestive of possible associations with fibroids. Women reporting a history of BV had somewhat elevated odds of both small and large fibroids.

Table 2. Adjusted Odds Ratios for Fibroids According to Self-Reported History of Reproductive Tract Infections

Reproductive tract infections	Fibroids: *Yes* N = *363* n *(%)*	Fibroids: *No* N = *1,293* n *(%)*	*Age-adjusted* OR (95% CI)	*Multivariable-adjusted* OR (95% CI)
Any RTI[a]				
Yes	262 (72)	910 (70)	1.05 (0.80–1.36)	1.15 (0.87–1.52)[b]
No	101 (28)	381 (30)		
Missing		2		
PID				
Yes	34 (9)	128 (10)	0.90 (0.60–1.35)	0.94 (0.62–1.43)[b]
No	329 (91)	1,164 (90)		
Missing		1		
Chlamydia				
Yes	125 (34)	503 (39)	0.85 (0.66–1.09)	0.92 (0.70–1.21)[c]
No	238 (66)	788 (61)		
Missing		2		
Bacterial vaginosis				
Yes	147 (41)	477 (37)	1.14 (0.89–1.45)	1.21 (0.93–1.58)[c]
No	216 (60)	815 (63)		
Missing		1		
Trichomonas				
Yes	116 (32)	414 (32)	0.90 (0.70–1.16)	0.90 (0.68–1.20)[c]
No	247 (68)	878 (68)		
Missing		1		
Gonorrhea				
Yes	62 (17)	261 (20)	0.81 (0.60–1.11)	0.94 (0.67–1.33)[c]
No	301 (83)	1,031 (80)		
Missing		1		
Genital herpes				
Yes	31 (9)	112 (9)	0.93 (0.61–1.42)	0.89 (0.58–1.39)[c]
No	332 (91)	1,180 (91)		
Missing		1		
Genital warts				
Yes	28 (8)	85 (7)	1.10 (0.70–1.73)	1.09 (0.68–1.74)[c]
No	335 (92)	1,207 (93)		
Missing		1		

Any ''prefer not to answer'' response was coded as missing.
[a]Includes pelvic inflammatory disease, chlamydia, bacterial vaginosis, trichomonas, gonorrhea, genital herpes, and genital warts.
[b]Logistic regression model adjusted for age (continuous), education, body mass index, alcohol, menarche, parity, Depo–Provera use.
[c]Logistic regression model adjusted for age (continuous), education, body mass index, alcohol, menarche, parity, Depo–Provera use, and other RTIs except PID and the RTI being evaluated.
CI, confidence interval; OR, odds ratio; PID, pelvic inflammatory disease; RTI, reproductive tract infection.

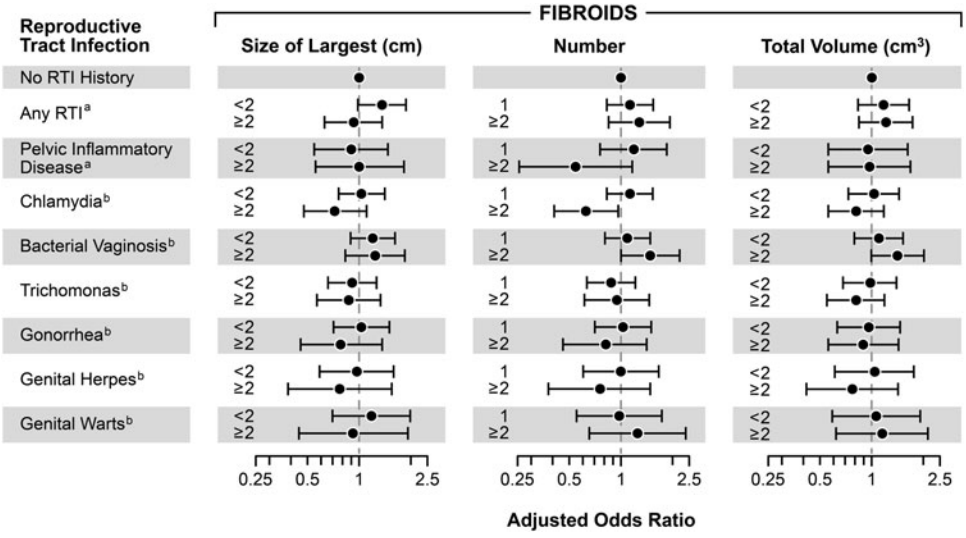

FIG. 1. Adjusted odds ratios for size of the largest fibroid, number of fibroids, and total fibroid volume according to self-reported history of reproductive tract infections. [a]Adjusted for age, education, body mass index, alcohol, menarche, parity, and Depo-Provera use. [b]Adjusted for age, education, body mass index, alcohol, menarche, parity, Depo-Provera use, and all other reproductive tract infections (RTIs) except pelvic inflammatory disease and the RTI being evaluated.

The associations were of borderline significance for two or more fibroids and for larger total fibroid volume ($\geq 2cm^3$). Although speculative, the tendency for increased odds with BV might be influenced by its chronic nature.[27,28] For those with a previous chlamydia diagnosis, the odds of having multiple fibroids (≥ 2) was significantly reduced. However, any mechanism for protection by chlamydia is unknown. In summary, our study results do not corroborate any of the suggestive increased odds of fibroids associated with self-reported histories of PID, chlamydia, trichomonas, or herpes previously described in smaller studies.[10,23]

This study has several limitations. It was a cross-sectional analysis with self-reported RTI diagnoses. Though the onset of fibroid development is unknown, over half of the women reported their first RTI diagnosis before the age of 20, while fibroid development in African Americans appears to be infrequent before the mid 20s.[29] Also, most of the fibroids were small suggesting relatively recent development. Finally, the median time between first RTI diagnosis and study enrollment was 9 years, again supporting the likelihood that exposure occurred before disease onset.

Self-reported data on history of RTI diagnosis may be subject to recall error.[30–33] However, the frequencies of RTIs in our sample are generally similar to those reported in other studies of African American women.[34,35] Perhaps a more important problem is that the majority of RTIs can often be asymptomatic, so even those who have not had a previous diagnosis may still have had or currently have an RTI. Some women also may have been tested and were positive but never received their results, did not understand them, or just did not report them (due to confidentiality concerns or social desirability bias). Because questions were asked via a self-administered CAWI questionnaire, social desirability bias should have been reduced.[36,37] The validity of our self-reported data is supported by our observation that both lower age at first sex and higher numbers of sex partners were associated with increased reporting of infection. Finally, our sample is not a representative population-based sample of women. However, because it captures early fibroid development (most of the women with fibroids had small fibroids), our sample was a relevant one for investigating the possible role of RTIs in the hypothesized fibroid pathogenesis involving aberrant tissue repair.[21,22]

Our study has several strengths. We used enrollment data from an ongoing prospective study with a standardized measure of fibroid status based on systematic ultrasound screening rather than fibroids clinically detected because of symptoms. The number, diameter, and volume of the fibroids were systematically measured, so we were able to examine associations with these separate characteristics. Twenty-two percent (22%) of our cohort of young African American women had fibroids at ultrasound screening, a prevalence which falls within the range of prior U.S. studies that conducted ultrasound screening.[2,10,29,38] Our sample size was sufficient to provide good precision for the main hypotheses. We also had extensive data to assess potential confounding, very minimal missing data, and we conducted sensitivity analyses to evaluate potential bias.

Conclusions

Overall, the studies of RTIs and fibroids, including ours, reveal no strong associations. Our study was the first to look at the relationship between RTIs and fibroid size, number and total volume, but most studies have been limited by the use of self-reported exposure histories of these often asymptomatic infections. The small study that looked for pathogens in fibroid tissue did no serological assessment to biochemically measure past exposure to infection.[10] Future studies are needed to take the next step and use serology to better investigate associations between RTIs and fibroids.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Donna Day Baird, PhD
Epidemiology Branch A3-05
National Institute of Environmental Health Sciences
National Institutes of Health
PO Box 12233
Research Triangle Park, NC 27709

E-mail: baird@niehs.nih.gov