

Cervical neoplasia–related factors and decreased prevalence of uterine fibroids among a cohort of African American women

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Objective: To investigate whether the previously reported inverse association between cervical neoplasia and uterine fibroids is corroborated.

Design: Cross-sectional analysis of enrollment data from an ongoing prospective study of fibroid development.

Setting: Not applicable.

Patient(s): Self-reported data on abnormal Pap smear, colposcopy, and cervical treatment were obtained from 1,008 African American women ages 23–34 with no previous fibroid diagnosis and no reported history of human papillomavirus vaccination. Presence of fibroids was assessed at a standardized ultrasound examination.

Intervention(s): None.

Main Outcome Measure(s): The association between the three cervical neoplasia–related variables and the presence of fibroids was evaluated with logistic regression to estimate age-adjusted and multivariable-adjusted odds ratios (aORs).

Result(s): Of the analysis sample, 46%, 29%, and 14% reported a prior abnormal Pap smear, colposcopy, and cervical treatment, respectively. Twenty-five percent had fibroids at ultrasound. Those reporting cervical treatment had a 39% (aOR, 0.61; 95% confidence interval [CI] [0.38–0.96]) reduction in fibroid risk. Weak nonsignificant associations were found for abnormal Pap smear and colposcopy.

Conclusion(s): Although a protective-type association of cervical neoplasia with uterine fibroids seems counterintuitive, a causal pathway is possible, and the findings are consistent with two prior studies. Further investigation is needed on the relationship between fibroids and cervical neoplasia and human papillomavirus–related mechanisms.

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Key Words: Uterine fibroids, cervical neoplasia, cervical treatment, abnormal Pap smear, colposcopy

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Uterine fibroids are one of the most common gynecologic conditions affecting women during their reproductive years (1).

Symptoms resulting from fibroids (pain, severe bleeding, reproductive problems) are the leading reason for hysterectomy in the United States, ac-

counting for 40% of all hysterectomies, or approximately 240,000 hysterectomies per year (2). One U.S. study found an estimated cumulative incidence of fibroid tumors by age 50 of >80% for African American women and close to 70% for white women (3). Pathology data based on a systematic search of 100 sequential hysterectomy specimens that were thinly sliced for analysis show comparable prevalence estimates (4).

The etiologic cause of fibroids is largely unknown, although selected risk factors have been established such as African American heritage,

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older age (up to the age of menopause), younger age at menarche, and nulliparity (5–7). Other factors such as body mass index (BMI), smoking, hormonal contraceptive use, and alcohol have been inconsistently associated with fibroid risk (5, 8, 9). A hypothesis was postulated decades ago that reproductive tract infections may play a role in fibroid development (10); however, there are limited data that examine associations between reproductive tract infections and fibroid risk (5).

One clinic-based case-control study found a positive association and dose-response relationship between pelvic inflammatory disease (PID), the number of PID episodes, and uterine fibroids among premenopausal women (11). No association was found between self-reported history of genital herpes or warts and fibroids, although a nonsignificant increased risk of fibroids was observed for women with self-reported history of *Chlamydia trachomatis* infection. The Uterine Fibroid Study found no association between PID and uterine fibroids for both African American and white women; positive nonsignificant associations for self-reported history of *Chlamydia* infection in white women; and trichomonas, syphilis, and “other infections” in African American women. A self-reported history of genital herpes was found to have a nonsignificant positive association in both ethnic groups (5). Interestingly, and counterintuitively, in both of these studies (5, 11), self-reported history of abnormal Pap smear was inversely associated with fibroids.

In the current study we explored the relationship between uterine fibroids and women’s reported history of abnormal Pap smears. We also investigated additional markers of cervical pathology that are even more closely linked to more severe stages of cervical neoplasia, colposcopy (a procedure performed after an abnormal Pap result to further examine the cervix and biopsy lesions), and treatment for cervical dysplasia (i.e., cone biopsy, loop excision, cryotherapy, or laser treatment conducted after colposcopy to remove or destroy abnormal cells).

MATERIALS AND METHODS

Study Participants

We used enrollment data from an ongoing study, the Study of Environment, Lifestyle and Fibroids (SELF). SELF is a prospective cohort study of fibroid development. From November 2010 to December 2012, the study enrolled a volunteer sample of approximately 1,700 African-American women ages 23–34 without a diagnosis of fibroids. Enrollment data are currently available for the first 1,199 participants. Recruitment was designed to saturate the recruitment area (Detroit, Michigan, and surrounding area) with information about the study. Materials included a website (detroitself.org); fliers; brochures at health care clinics; local radio, television, newspaper, and magazine advertisements; information booths at community events; and letters to women who had been seen in the past year by a doctor at the Henry Ford Health System (HFHS), a large medical provider in the Detroit area and collaborating institution. The letters were sent to women listed as 23–34 years of age, with stratification by age to help maintain equal recruitment by age. This age group was chosen on the basis of ultrasound

screening data (12) to capture women early enough to have a sizeable proportion without fibroids.

Women who were interested in learning more about the study phoned the study number and could be screened for eligibility. 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. Eligible women with further interest received detailed information about the study during an orientation session. Those who chose to enroll after the orientation gave informed consent and completed self-administered questionnaires and a telephone interview and had a standardized research ultrasound examination to screen for the presence of fibroids. Some women had uterine fibroids at enrollment of which they were unaware.

Women pregnant at recruitment are delayed enrollment until 4 months after delivery so that pregnancy does not interfere with ultrasound assessment of fibroids. SELF participants will be followed for at least 5 years after enrollment with subsequent ultrasound examinations every 20 months. Women who screened negative at enrollment will be followed for fibroid development; women who screened positive at enrollment and those who develop incident fibroids will be followed for development of additional fibroids and fibroid growth. The study was approved by the institutional review boards of the National Institute of Environmental Health Sciences and HFHS.

Study participants were excluded if they reported being vaccinated with at least one human papillomavirus (HPV) shot (three are given for full protection; $n = 191$, 16%). These women would be less likely to have a history of cervical neoplasia since it is highly linked to HPV infection. Thus, 1,008 participants were eligible for this analysis. The women who were ineligible differed from eligible participants in regards to age. Those reporting at least one HPV shot were younger than those reporting no shots, which is expected since the HPV vaccine has been recommended since 2006 for women 26 and younger.

Cervical Neoplasia-Related Variables

Three cervical neoplasia-related variables were evaluated in this study: self-reported previous abnormal Pap smear (yes/no), colposcopy (yes/no), and colposcopy follow-up with cervical treatment, that is, cone biopsy, loop electrosurgical excision procedure (LEEP), cryotherapy, or laser treatment (yes/no). Women were not asked to report the specific findings of the abnormal Pap smears or colposcopies, nor were they queried about history of endometrial curettage. Participants could only answer questions regarding cervical treatments if they answered yes to having had either a previous abnormal Pap smear or colposcopy.

Fibroid Assessment

The outcome for this study was fibroid presence (yes/no) at the transvaginal ultrasound examination completed at enrollment. Ultrasound is the standard procedure for the detection

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