

The prevalence of migraines in adolescents with endometriosis

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Objective: To determine the prevalence and experience of migraines in adolescents with surgically confirmed endometriosis compared with those without endometriosis.

Design: Cross-sectional study conducted within The Women's Health Study: From Adolescence to Adulthood—an ongoing longitudinal cohort.

Setting: Boston Center for Endometriosis.

Patient(s): Adolescent females enrolled November 2012 through November 2016. The case group included adolescents surgically diagnosed with endometriosis. The control group included adolescents without endometriosis, recruited from the local community and clinics.

Intervention(s): Not available.

Main Outcome Measure(s): An extensive online health questionnaire regarding medical history, lifestyle, medication use, anthropometrics, and symptom experience and treatments. Migraine diagnosis was self-reported. Migraine pain and noncyclic pelvic pain severity were rated using an 11-point numerical rating scale. Cyclic pelvic pain was categorized.

Result(s): Adolescents with endometriosis were more likely to experience migraines (69.3%) than those without endometriosis (30.7%) (multivariable odds ratio = 4.77, 95% confidence interval 2.53, 9.02). For each 1-point increase in the migraine numerical rating scale, the odds of endometriosis increased by 22% (multivariable odds ratio = 1.22, 95% confidence interval 1.03, 1.44; $P_{\text{trend}} = .02$). Among those with endometriosis, age of menarche was associated inversely with the odds of migraines. Participants with endometriosis and migraines have more dysmenorrhea than those without migraines.

Conclusion(s): Adolescents with endometriosis are more likely to experience migraines than adolescents without endometriosis. A linear relationship exists between migraine pain severity and the odds of endometriosis, suggesting heightened pain sensitivity for adolescents with endometriosis. Due to the strong correlation, patients who present with either condition should be screened for comorbidity to maximize the benefits of care. (Fertil Steril® 2017; ■: ■–■. ©2017 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, adolescents, migraines, pain sensitization, WERF EPHeCt

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Endometriosis is a gynecological disease in which endometrium-like tissue grows in locations outside of the uterus, primarily in the pelvic cavity. Notable symptoms include pelvic pain, dysmenorrhea, menorrhagia,

and infertility (1, 2). Migraine is another pain disorder that involves headaches, frequently accompanied by nausea, fatigue, phonophobia, and photophobia (1, 3). Both disorders can impede productivity and cause moderate-to-

severe pain that intensifies through routine physical activity (1).

In adults, these two pain disorders have been linked, as migraines appear to occur more commonly in patients with endometriosis than in the general population (1,3–5). This association may be because women with chronic pelvic pain (CPP) often have hypersensitivity to pain, known as central sensitization (6–8). Pain sensitivity may be heightened for those patients with endometriosis compared with those without. Similar studies exploring endometriosis and migraine co-occurrence have not yet been replicated within the adolescent population.

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The current study was conducted to determine the prevalence of migraines in adolescents with surgically confirmed endometriosis compared with those without endometriosis. We hypothesized that the prevalence of migraines would be higher in those with endometriosis. In addition, we hypothesized that among participants with migraines, those with endometriosis would have worse migraine pain than participants who did not have endometriosis. We also sought to determine whether adolescents suffering from both endometriosis and migraines experienced more severe pelvic pain than those with only endometriosis.

MATERIALS AND METHODS

This cross-sectional study was set within an ongoing longitudinal cohort study, The Women's Health Study: From Adolescence to Adulthood, enrolling premenopausal females aged ≥ 7 years with and without surgically confirmed endometriosis. This study is conducted within the Boston Center for Endometriosis, which is a joint initiative between Boston Children's Hospital and Brigham and Women's Hospital, with the primary aim of investigating endometriosis across the lifespan. Participants are recruited from the two tertiary care centers, as well as from the surrounding community by local advertisements, online postings, and word of mouth. The participants completed an extensive baseline questionnaire and annual follow-up questionnaires. Our extensive online health questionnaire is an expanded version of the World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project (WERF EPHeCT) standard clinical questionnaire (9). Surveys are collected and managed using REDCap electronic data capture tools. The study was approved by the Boston Children's Hospital Institutional Review Board on behalf of Boston Children's Hospital and Brigham and Women's Hospital. Informed consent with obtained, with parental consent/participant assent for girls < 18 years.

The analytic population for the current study included female adolescents who were enrolled from November 2012 through November 2016, and completed the baseline questionnaire. Participants who had been surgically diagnosed with endometriosis at the hospital of enrollment comprised the case group (10). Participants in the control group included healthy individuals and those with other medical comorbidities who were recruited from the local Boston community and from clinics at Boston Children's Hospital and Brigham and Women's Hospital. The control subjects were not undergoing evaluation for endometriosis and had no surgical diagnosis of endometriosis. As part of study enrollment, participants were asked to complete a survey soliciting information regarding menstrual history (including age at menarche), medical history, lifestyle, medication, anthropometric, and environmental exposures, as well as symptom experience and treatments. Those participants who failed to complete the pelvic pain symptom portions of the questionnaire were excluded from this analysis ($n = 16$). The remaining participants were restricted to those who were children and adolescents (aged ≤ 21 years) at enrollment ($n = 391$).

The primary characteristics of interest included having ever experienced migraines, with or without a diagnosis from a physician, age at migraine diagnosis, migraine pain severity, and the presence and severity of cyclic and noncyclic pelvic pain, as well as lower general abdominal pain. Migraine pain and noncyclic pelvic pain severity were rated using an 11-point numerical rating scale anchored with 0 = no pain and 10 = worst imaginable pain. Cyclic pelvic pain severity was categorized as no pain, mild (medication never or rarely needed), moderate (medication usually needed), or severe cramping (medication and bed rest needed). Information was also collected regarding the age of pelvic pain and/or migraine pain onset, age at diagnosis of endometriosis and/or migraine, hormonal medications ever used, and smoking history. In addition collected covariates from the questionnaire included participants' demographic data such as age, race, body mass index (BMI), and educational level.

We initially calculated crude odds ratios (ORs) and 95% confidence intervals (CIs) using univariate unconditional logistic regression. We then used adjusted models, first including covariates for age (continuous), race (white, black, Asian, other/missing), and whether or not the participant ever used hormonal medication (never/ever). Second adjusted models also included terms for the presence and degree of menstrual pain (none/mild or moderate/severe) and for the presence of general, noncyclic pelvic pain (yes/no). We examined the association between endometriosis and risk of migraine overall and the association between migraine symptoms (pain severity and age at diagnosis) and risk of endometriosis. Pain severity and age at menarche were modeled categorically and continuously. In addition, we examined the association between age at menarche, pelvic pain, and migraine risk, separately in endometriosis cases and noncases. To examine heterogeneity in the relation between age at menarche or pelvic pain and migraine risk by endometriosis status, we ran logistic regression models and calculated likelihood ratio tests comparing models fit with and without interaction terms. Analyses were completed with SAS version 9.4 (SAS Institute).

RESULTS

The participants in this study included 296 cases and 95 controls, comprised of 205 adolescents with both endometriosis and migraines, 91 adolescents with only endometriosis, 30 adolescents with only migraines, and 65 adolescents with neither endometriosis nor migraines. On average, the participants were primarily in school with an average age of 17.4 years ($SD = 2.3$; Table 1). In all four categories, most participants were of normal BMI category (compared with underweight, overweight, or obese). Most participants were of white race (79.8%), although there was a higher ratio of black, Asian, and other races among those participants with only migraines or neither disorder. As would be expected due to clinical history, 92.2% of adolescent participants with endometriosis had ever taken hormonal medication compared with 54.7% of adolescents without endometriosis. There was an increased prevalence of anxiety and mood disorders among those with compared with those without endometriosis.

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