GENERAL GYNECOLOGY

Early menstrual characteristics associated with subsequent diagnosis of endometriosis

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OBJECTIVE: The aim of this study was to investigate the association between early menstrual characteristics, before symptom onset, and later diagnosis of endometriosis.

STUDY DESIGN: This was a case-control study of 268 Australian women with surgically confirmed moderate-to-severe endometriosis (cases) and 244 women without endometriosis (controls). Early menstrual cycle characteristics, before age at symptom onset, were analyzed.

RESULTS: Menarche after age 14 years was strongly and inversely associated with endometriosis (odds ratio, 0.3; 95% confidence interval, 0.1–0.6). A history of dysmenorrhea was associated with subsequent endometriosis (odds ratio, 2.6; 95% confidence interval, 1.1–6.2). Despite a suggestive trend, shorter menstrual cycle length was not associated with endometriosis. Duration of natural menstruation and heaviness of flow were not associated with subsequent risk of endometriosis; neither was the reported type of sanitary protection used nor history of sexual intercourse during menstruation.

CONCLUSION: There is a decreased risk of endometriosis with late age at menarche and an increased risk in women who report an early history of dysmenorrhea.

Key words: dysmenorrhea, early menstrual characteristics, endometriosis, etiology, menstruation

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Endometriosis is a common benign gynecologic disorder, defined as endometrial tissue occurring outside its normal location in the uterus.[1] Pelvic endometriosis is the most common form of the disease, and it mostly affects women during their reproductive life.[2] The prevalence of endometriosis is thought to approach 10–15% in the general female population and up to 35–50% in women who experience pelvic pain, infertility, or both.[3]

The pathogenesis of endometriosis is commonly described using Sampson's theory, which proposes that ectopic endometrium and potentially viable, steroid-sensitive cells are fluxed backward through the fallopian tubes into the peritoneal cavity during menses.[4] The popularity of this theory has meant that much of the existing epidemiologic research on endometriosis has focused on menstrual cycle characteristics.[5-7] In particular, increased exposure to menstruation in terms of short cycle length, long duration of flow, and low parity have frequently been identified as possible risk factors.[8] However, the epidemiologic findings have been inconsistent, with effect estimates varying widely.[5,9-11] Furthermore, it has been postulated that many of the supposed menstrual risk factors for endometriosis are in fact consequences of the disease,[12] because the disease is often characterized by symptoms of severe dysmenorrhea, dyspareunia, menorrhagia, and irregular menses.[13,14]

A major shortfall in studies of endometriosis that have evaluated potentially causative exposures that change over time, such as menstrual cycle length, is that only recent menstrual characteristics have been collected rather than adolescent or early adulthood menstrual characteristics preceding disease occurrence in affected women.[12] The potential role of menstrual cycle characteristics in the actual development of endometriosis therefore remains an open question. The aim of the current study was to further examine the role of atypical menstrual history and symptoms in the development of endometriosis, with particular emphasis on the timing of potential causal exposures. We hypothesized that women with endometriosis would more likely have had an early age at menarche, shorter cycle lengths, and heavier menstrual flow compared with women without endometriosis. We also hypothe-

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sized that a prior history of longer menses, tampon use, and sexual intercourse during menstruation were risk factors for endometriosis.

Our detailed data collection allowed for the analysis of early exposure data, before the onset of symptoms rather than diagnosis, because the magnitude of the average delay between onset of symptoms and diagnosis of endometriosis is in the order of 5–7 years.[15,16]

MATERIALS AND METHODS

Study population and sample

This Australian case-control study included women aged between 18–55 years with surgically confirmed endometriosis; full study details of study design and participant recruitment have been reported previously.[17] The cases were initially recruited largely through media campaigns between 1996–2002 for a genetic study of endometriosis.[18] Although the primary objective of the genetic study was to recruit affected sibling pairs for linkage studies, the extensive media exposure for this study resulted in recruitment of approximately 970 surgically diagnosed women who had no affected sibling. From this group of women we identified those with moderate/severe disease (rAFS stages III/IV) and no first-degree relative who had endometriosis diagnosed, and this made up the pool from which eligible cases were drawn for this study.[19,20] A total of 310 potential cases were randomly selected and all were invited to participate. Of these, 2 were found to be ineligible, as they were residing overseas at the time of contact, and an additional 7 were unable to be contacted. Of the remaining 301 eligible cases who were contacted, 268 agreed to participate (89%).

Potential control participants were same-sex female twin pairs enrolled with the Australian Twin Registry. They reported never having endometriosis diagnosed in earlier twin studies.[21] Controls were randomly selected from women frequency-matched to the cases on age (5-year groups) and geographic location (urban/rural). In all, 511 women were contacted. Of these, 40 were ineligible, because they were residing overseas (n = 11) or had a new diagnosis of endometriosis (n = 29), and a further 39 were unable to be contacted. Of the 432 eligible women, 244 (57%) agreed to participate and returned a questionnaire.

Data collection and exposures

Information was collected using a self-administered questionnaire, which included questions about demographic, hormonal; and reproductive factors; physical characteristics; and lifestyle habits. To determine the influence of the timing of relevant exposures, data were collected in prespecified age bands: before age 10 years, 10–19 years, 20–29 years, 30–39 years, and 40+ years. The early menstrual cycle characteristics of interest included age at menarche, cycle length, heaviness of flow, duration of natural menstruation (not while using oral contraceptives), and pelvic pain in association with menstruation. In addition, we collected information about the type, frequency, and timing of sanitary protection, as well as information about sexual intercourse during menstruation. Data for some menstrual cycle characteristics were incomplete, because some women could not remember details of their menstrual cycles in past years. In addition, it was difficult to distinguish menstrual characteristics from disease symptoms for some affected women, because symptoms of endometriosis started in the 10–19 year age range, which is the typical age range for onset of menstruation. Those women for whom menstrual characteristics and symptom onset were both recorded in the 10–19 year age range were excluded from this analysis.

Ethics approval for the study was obtained from the Queensland Institute of Medical Research (QIMR) Human Research Ethics Committee (ref: H0005-00-016), the Australian Twin Registry (ref: 96-007-3), and the University of Queensland's Medical Research Ethics Committee (ref: H313).

Statistical analysis

Unconditional logistic regression was used to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for the association between menstrual characteristics and endometriosis risk. The analyses of exposure before onset of symptoms were conducted using self-reported age of onset of endometriosis as the cutoff. For controls, the self-reported age of onset of endometriosis of their matching case was used as the corresponding cutoff point. Multivariable logistic models were used to adjust for potential confounders, including state of residence; age at menarche; body size (at 10 years and 16 years); and menstrual cycle characteristics, such as length, regularity, and heaviness of menstrual flow. For consistency in the multivariate analysis, the same period of exposure was used for both the exposure of interest and other confounding variables included in the model (eg, ORs calculated for a particular exposure relating to the time before onset of symptoms were adjusted for confounding variables also related to the period before onset of symptoms). Power calculations based on a 1:1 case control design and a 2-sided alpha of .05, using our recruitment figures of 268 cases, indicate a power of 93% to detect an OR of 2.0 and a power of 79% to detect an OR of 1.75, for an exposure prevalence of 20% in the control group. The SPSS statistical package version 12.0 was used for all data analysis (SPSS, Inc, Chicago, IL).

RESULTS

Two hundred sixty-eight women with moderate-to-severe endometriosis and 244 controls were included in the study. Cases were more likely to have been residing in the state of Queensland, where the study was based, whereas controls were mainly based in Victoria, where the Australian Twin Registry is based, and nearby Tasmania ($P < .001$) (Table 1). A higher proportion of cases were of Asian, African, and Southern and Eastern European descent ($P = .04$), and cases were less likely to have completed 15 or more years of schooling ($P = .002$) compared with controls. Cases did not differ from controls with regard to marital status, religion, smoking status, or alcohol consumption (Table 1).

Table 2 shows the association between menstrual cycle characteristics and en-