Risk factors for deep endometriosis: a comparison with pelvic and ovarian endometriosis

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Objective: To assess whether deep endometriosis has different risk factors compared with endometriosis at other sites. In epidemiological terms, this should be the case if deep endometriosis represents a different condition than ovarian and peritoneal endometriosis.
Design: Case-control study.
Setting: University hospitals.
Patient(s): The first group of cases included 181 women with a diagnosis of deep endometriosis. The second group of cases included 162 women with endometriosis at other sites. The control group included women younger than 55 years of age who were admitted for acute non-gynecological, non-hormonal, non-neoplastic conditions.
Intervention(s): Questionnaire.
Main Outcome Measure(s): Odds ratios.
Result(s): The age distribution of women with cases of deep and ovarian and pelvic endometriosis was not statistically significantly different. A higher body mass index decreased the risk of both deep as well as ovarian and pelvic endometriosis: the estimated ORs for women reporting a body mass index of $\geq$21 vs. those reporting a body mass index of <21 were 0.6 (95% confidence interval [CI], 0.3–0.8) for deep endometriosis and 0.6 (95% CI, 0.4–0.9) for pelvic and ovarian endometriosis. Parous women were at decreased risk: in comparison with nulliparae, the odds ratio for deep endometriosis was 0.1 (95% CI, 0.1–0.2) for women reporting one or more births. The corresponding value for pelvic and ovarian endometriosis was 0.1 (95% CI, 0.1–0.2).
Conclusion(s): This study suggests that deep as well as ovarian and pelvic endometriosis share similar risk factors. (Fertil Steril® 2008;90:174–9. ©2008 by American Society for Reproductive Medicine.)

Key Words: Case-control study, deep endometriosis, risk factors

Endometriosis is a common gynecological disease (1). Despite its relatively high prevalence, little is known about its epidemiology and etiology (2).

The reflux hypothesis commonly has been suggested to explain the etiology of peritoneal endometriosis.

Recently, great attention has been focused on deep endometriosis. Deep endometriosis is characterized by a stronger relation with pelvic pain and dyspareunia than are cases of endometriosis in other anatomical sites (3). These clinical characteristics have suggested that deep endometriosis may have different etiopathologic mechanisms in comparison with pelvic and ovarian endometriosis (4, 5).

For example, it has been suggested that deep lesions of the posterior cul de sac originate from metaplasia of Müllerian remnants located in the rectovaginal septum, thus constituting an entity different from peritoneal endometriosis (4). Alternatively, these forms could be the most severe manifestation of the peritoneal disease (6).

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In epidemiological terms, if deep endometriosis represents a different condition, it should recognize different risk factors in comparison with endometriosis at other sites. Few data are available on risk factors for endometriosis in different sites (7, 8). Some studies have shown no difference between pelvic and ovarian endometriosis, but the epidemiological profile of deep endometriosis is substantially unknown.

To obtain information, we have analyzed data on risk factors collected in a case-control study. Cases considered in this article have not been included in previous publications.

MATERIALS AND METHODS

The present analysis included data collected in a case-control study. The first group of cases included 181 women younger than 55 years of age (median age, 34 y; range, 26–48 y) who had a first laparoscopically confirmed diagnosis of deep endometriosis (incident cases) and had been admitted to the obstetrics and gynecology departments of the University of Verona during the period from 2001 to 2002 or to the obstetrics and gynecology department of San Paolo hospital, University of Milan, during the period from November 2003 through October 2005.

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Deep endometriosis was defined as endometriosis that infiltrates >5 mm under the peritoneal surface (6). The depth of infiltration was assessed during laparoscopy or laparotomy or by vaginal or rectal ultrasound examination. A total of 57 cases presented both deep endometriosis and endometriosis at other sites; they were included in this group in consideration of the peculiarity of this site of endometriosis.

The second group of cases included 162 women with pelvic and ovarian endometriosis but without deep endometriosis. They were the first women younger than 55 years of age (median age, 33 y; range, 20-55 y) who had a first laparoscopically confirmed diagnosis of endometriosis without deep lesions that was observed after the identification of a case to the same obstetrics and gynecology department at which the case was identified.

The surgical procedures for the diagnosis of endometriosis were performed under the supervision of the same team in both the participating centers. For each woman with endometriosis, data on stage and site of endometriosis were collected.

The control group includes women younger than 55 years of age who were admitted for acute non-gynecological, nonhormonal, non-neoplastic conditions to several university departments. They were recruited as control women in a case-control study of female genital neoplasms (9). A total of 1,627 control women was identified. Of this total, 329 (median age, 34 y; 20-55 y) were randomly selected within strata of 5-year age groups and calendar year at interview. Of these, 31% were admitted for traumatic conditions (mostly fractures and sprains); 23% had nontraumatic orthopedic disorders (mostly low back pain and disc disorders); 12% had acute abdominal diseases requiring surgery; and 34% had other miscellaneous illnesses, such as disorders of the ear, nose, throat, or teeth.

Trained interviewers identified and questioned case patients and control women, and all interviews were conducted in hospital. Fewer than 3% of case patients and control women refused to be interviewed. Information was obtained, by using a structured questionnaire, on general sociodemographic factors, personal characteristics and habits, and gynecological and obstetric history.

Because of the sample size of the study, we were able to identify, for cases with deep or ovarian and pelvic endometriosis, odds ratios of ≥ 2 for factors that had a frequency in the control group of about 10% or more.

Data Analysis

We computed ORs as estimators of relative risks and the corresponding 95% confidence intervals (CIs) for deep endometriosis and for pelvic and ovarian endometriosis separately vs. the control group.

To account simultaneously for the effects of several potential confounding factors, we performed unconditional multiple logistic regression, with maximum-likelihood fitting, to obtain the ORs for endometriosis (10). The variables included in the model were age, study center, and calendar year at interview.

RESULTS

The distribution of case patients and control women according to age, site, and stage of endometriosis as well as selected characteristics is presented in Table 1. The age distribution of cases with deep and pelvic and ovarian endometriosis was not statistically significantly different.

More educated women were at higher risk of both deep as well as pelvic and ovarian endometriosis. In particular, the estimated ORs, in comparison with women reporting a primary- or intermediate-school degree, were 2.9 (95% confidence interval [CI], 1.9–4.5) and 2.0 (95% CI, 1.3–3.1), respectively, for deep and for pelvic and ovarian endometriosis for women reporting a high-school degree and were 4.9 (95% CI, 2.8–8.0) and 5.8 (95% CI, 3.4–10.1) for women reporting a university degree.

Higher body mass index (BMI) and ever smoking decreased the risk of both deep and pelvic ovarian endometriosis. In particular, the estimated ORs for women reporting a BMI (in kg/m^2) of ≥ 21 vs. those reporting a BMI of <21 were 0.6 (95% CI, 0.3–0.8) for deep endometriosis and 0.6 (95% CI, 0.4–0.9) for pelvic and ovarian endometriosis. The corresponding values for current and former smokers vs. never smokers were 0.6 (95% CI, 0.4–0.8) and 0.5 (95% CI, 0.3–0.8), and 0.7 (95% CI, 0.4–1.4) and 0.7 (95% CI, 0.4–1.4).

No association emerged between marital status and risk of deep or of pelvic and ovarian endometriosis.

Menstrual and reproductive history parameters for the patients are summarized in Table 2. Age at menarche and lifelong type of menstrual cycles were not related to the risk of deep or pelvic and ovarian endometriosis. Parous women were at decreased risk: in comparison with nulliparae, the odds ratio (OR) for deep endometriosis was 0.1 (95% CI, 0.1–0.2) for women reporting one or more births. The corresponding value for pelvic or ovarian endometriosis was 0.1 (95% CI, 0.1–0.2).

In an attempt to minimize and analyze the effect of selection and detection bias, we computed OR of deep endometriosis and other sites separately for indication for surgery (sterility; pelvic pain; and other reasons, including pelvic masses and incidental diagnosis). No difference in the results emerged (data not shown).

We have further analyzed separately the role of factors that have been found to be significantly associated with the risk of endometriosis for women with cases of ovarian, pelvic, ovarian and pelvic endometriosis, and deep endometriosis with and without endometriosis on other sites.

With regard to education, the ORs for endometriosis for women with a university degree, in comparison with women