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Characteristics of women with endometriosis from the USA and Puerto Rico

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Abstract

Purpose—To describe lifetime differences in clinical characteristics of women with endometriosis between the USA and Puerto Rico.

Methods—A descriptive study using self-administered demographic and clinical questionnaires was undertaken. Women with self-reported surgically diagnosed endometriosis who completed questionnaires from the Endometriosis Association (EA), Wisconsin, USA (n = 4358) and the Endometriosis Research Program (ERP) in Puerto Rico (n = 878), were included in this study. We compared demographic, gynecological and clinical history, frequency of endometriosis-associated symptoms and co-morbidities.

Results—Although both groups have similar symptomatology, EA respondents had significantly higher rates of chronic pelvic pain and incapacitating pain than ERP participants. EA respondents were significantly more likely to report a history of problems getting pregnant, heavy bleeding, and hysterectomy than ERP respondents. Miscarriages were more frequently reported by the ERP group. Co-morbidities such as allergies, chronic fatigue syndrome, and fibromyalgia were more prevalent in EA respondents, whereas asthma was significantly more frequent in participants from ERP.

Conclusions—Overall, women with endometriosis from the USA and Puerto Rico reported high rates of pain and infertility and a similar spectrum of symptoms. Those from the EA reported longer time to diagnosis, and diagnostic delays than those from the ERP, which may explain the

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observed increased in rates of endometriosis-related symptoms and co-morbidities in EA as compared to ERP.

Keywords

Endometriosis; Infertility; Pain; Co-morbidity; Epidemiology; Disparities

Introduction

Endometriosis affects 10% of the female population in the USA during their reproductive years, with an incidence of 2%–4% (1–3). Prevalence rates also vary according to the characteristics of the population studied: in asymptomatic women, prevalence ranges from 2%–22%; in infertile women, up to 40%; 6% in women undergoing sterilization, and up to 45% in patients with chronic pelvic pain (4, 5). Data on differences in prevalence of endometriosis across ethnic groups are limited. The Nurses' Health Study reported a 40% lower rate of diagnosed endometriosis among African-American or Hispanic women compared to Caucasians after adjusting for access to care (6). In Puerto Rico, the prevalence of endometriosis was estimated at 5%, although a high number of non-diagnosed reported suffering from incapacitating pelvic pain (7).

The most common symptoms of endometriosis are chronic pelvic pain, dysmenorrhea, dyspareunia and infertility, but women with endometriosis also report diverse nonspecific symptoms, making endometriosis a heterogeneous condition (8, 9). Also, co-morbidities such as endocrine and autoimmune disorders are more frequently reported by women with endometriosis than from the general female population (10, 11). There are studies describing the characteristics of women with endometriosis in two different populations, but only a few have investigated the demographics, menstrual-obstetric histories, and symptomatology of endometriosis patients from different geographic regions or ethnicities. One study with similar patient demographics and characteristics in women with endometriosis in the USA and the United Kingdom (UK) reported significant differences including early age at diagnosis, less frequency of contraceptive use, and best therapy success among patients (12). Another study reported a better response to therapy in Caucasian, as compared to Asian populations (13). More comparative studies are needed to identify possible differences among patients from differing geographic areas and ethnicities to confirm whether endometriosis is a 'universal' disease or whether there are population-specific patterns in the clinical presentation, prevalence of symptoms, approach to treatment, and clinical course. The aim of this study was to explore self-reported data about endometriosis-related and co-existing symptoms, and comorbidities in women with endometriosis from the USA and Puerto Rico.

Materials and methods

This descriptive study was performed using questionnaire responses from the Endometriosis Association (EA) patient registry, with Headquarters in Milwaukee, Wisconsin, USA, and the Endometriosis Research Program (ERP) at Ponce Health Sciences University (PHSU), in Ponce, Puerto Rico. The two groups of patients included members of the EA (predominantly

from the USA and mainly Caucasian) and patients who were recruited by a research program in Puerto Rico (all Hispanic).

The EA educates (through brochures, newsletters, DVDs, and books) and supports patients and their families (via support groups, networks, prescription discounts), and also funds and facilitates research on this condition. For this purpose, during 1998, the EA sent ~10,000 surveys via regular mail, to all of their membership, mainly from the USA (95%) and Canada (5%). The details of the methodology and design of the EA study have been previously described (11, 14, 15). The ERP registry consists of data from women with self-reported surgically confirmed endometriosis from Puerto Rico, collected from 2001–2008. Cases were recruited in collaboration with local gynecologists, Ob-Gyn residency programs and a patient support group. The details of the ERP study design and methodology have been described elsewhere (16). Both groups include previously and newly diagnosed women. For the EA group, calendar years of diagnosis ranged from 1956–1998 (with most diagnosed from 1985–1997); for the ERP group, diagnosis ranged from 1978–2008 (with most diagnosed from the mid-1990s to 2008).

Analyses were restricted to respondents with self-reported, surgically diagnosed endometriosis as indicated by responses regarding the diagnosis and use of surgical procedure (e.g., laparoscopy, laparotomy or hysterectomy) in both groups. Data from the EA and ERP questionnaires were de-identified and anonymized, and were approved for study by the National Institutes of Health Office of Human Subjects Research and the PHSU institutional review board (IRB).

The EA and the ERP questionnaires were self-administered and inquired about demographics, gynecological and obstetric history, endometriosis symptoms, co-existing symptoms, treatments for endometriosis, and other general lifestyle and family clinical history. The questionnaires were matched on similar questions (i.e., those asking the same concept with comparable response choices). Questions that were not present in both questionnaires, those with open text responses, or questions that asked the same concept but answers were not comparable were excluded from analyses. Some variables were re-coded (e.g., age at onset of symptoms asked as a numerical variable as in the ERP questionnaire versus choice of age categories in the EA questionnaire) to enable comparisons.

Other data were computed, including age at diagnosis by subtracting the year of birth from year of surgery for diagnosis, time to diagnosis using age of onset of symptoms relative to age at surgical diagnosis, and years with endometriosis based on year at survey completion compared relative to year of diagnosis. For computing time to diagnosis in the EA group, the categorical ages for onset of symptoms were converted to numerical values using their mid-point values (i.e., 12 for <15 yrs, 17 for 15–19 yrs, 22 for 20–24 yrs, 27 for 25–29 yrs, 32 for 30–34 yrs, 37 for 35–39 yrs, 42 for 40–44 yrs, and 47 for >45 yrs) following methods previously reported (11). Also, age at first live birth delivery for the EA group was computed based on the birthdate of the mother (survey respondent) and her first child's birthdate. Delivery age at first birth was reported by the survey respondents in the ERP group. This variable applied only to those women who reported having any live births, excluding those with missing/uninterpretable responses or other pregnancy outcomes (i.e., miscarriage).

Data were excluded from the analysis whenever the computed value could not be interpreted (e.g., time to diagnosis was a negative value). The following characteristics were comparable: method of diagnosis, age (at completion of survey), education level, age at onset of symptoms, pain characteristics and other symptoms, gynecologic and obstetric history, age at first live birth, prevalence of selected self-reported (and physician-diagnosed for the EA group) co-morbidities, and age at diagnosis and time to diagnosis.

Data from both questionnaires were collected independently and were analyzed by SAS[®] Software version 9.2 (SAS Institute, Inc., Cary, NC). Patient characteristics were described using frequency distributions and simple descriptive statistics, and are reported as percent (%) or means \pm standard deviations (SD). Nominal data were compared using chi-square or Fisher's exact tests; and t-tests or Wilcoxon rank-sum tests, as appropriate, were used to compare continuous data between groups. Pearson's correlation coefficient or Spearman's rho, as appropriate, were used for assessing relations between variables. Logistic regression analysis was used to adjust for the potential confounding effect of pertinent covariates, such as current age, age at surgical diagnosis, age at first live birth, time to diagnosis, years with endometriosis, or calendar timing of surgical diagnosis, as applicable. A two-sided p-value <0.05 was considered statistically significant.

Results

Of 5623 women completing questionnaires, a total of 5236 (93.1%) had self-reported, surgically diagnosed endometriosis, with 4358 (83.2%) responding to the EA survey and 878 (16.8%) from the ERP. The definition of self-reported surgically diagnosed endometriosis relied on responses to two questions in both surveys: 1) if it was definitely diagnosed, and 2) that it was diagnosed surgically. Of the 4745 EA respondents, 207 were excluded due to missing or suspicious endometriosis diagnosis and 180 were excluded because their diagnosis was not surgical. No one from ERP was excluded.

Subject demographics are presented in (Tab. I). Women from the EA were 3.6 years older than those from ERP ($p<0.0001$) and attained a higher level of education. Although the groups differed significantly with regards to education, over half of the participants from both populations had at least a Bachelor's degree. In general, the EA group reported onset of first pelvic symptoms at younger ages than the ERP group, notably before age fifteen.

Surgical diagnosis of endometriosis occurred during different decades for each group, with the ERP cohort being diagnosed generally more recently than the EA group as the year of diagnosis ranged from 1956 to 1998 for women in the EA, and 1978 to 2009 in the ERP cohort. Age at diagnosis was slightly older for those in the USA ($p<0.001$), who also reported longer times to diagnosis from onset of symptoms (11.3 ± 7.6 vs. 6.9 ± 7.2 , $p<0.001$) and a longer duration of living with diagnosed endometriosis at the time of the survey (6.9 ± 5.4 vs. 4.0 ± 5.2 , $p<0.001$).

Endometriosis-related pain and bleeding symptoms were all more frequently reported by women in the EA than the ERP group (Tab. II), despite considering the effects of pertinent

co-variates. In the ERP group, those with profuse bleeding were more likely to report having incapacitating pain as compared to EA group (74.7% vs. 62.4% respectively, $p = 0.04$).

Women from EA reported fewer pregnancies than the ERP (45% vs. 50%, $p = 0.012$); as would follow, live births were also less prevalent in the EA group than ERP (31% vs. 41%, $p < 0.001$). Women from the ERP group were statistically significantly younger than those from the EA at the time of delivering their first child (23.1 ± 4.9 vs. 28.0 ± 5.5 years, respectively, $p < 0.001$). For both groups, age at first birth was mildly positively correlated with duration of endometriosis (EA $r_s = 0.202$, $p < 0.001$; ERP $r_s = 0.231$, $p < 0.001$), but not with age at diagnosis or time to diagnosis. The difference in age at first birth did not affect the observed difference in the proportions reporting problems getting pregnant (Tab. II), which was more common in women in the EA group than ERP (69% vs. 53%, respectively, $p < 0.001$). However, miscarriages were more frequently reported by ERP group (21% vs. 14%, $p < 0.001$). Those with problems getting pregnant were not related to those reporting miscarriage in either group.

The most common co-existing symptom in both groups was back and leg pain. Gastrointestinal symptoms of diarrhea and nausea/vomiting were reported by twice as many women in the EA group compared to the ERP group ($p < 0.001$), among other symptoms. Adjusting for pertinent covariates, only the prevalence of fibroids and hysterectomies were not significantly different between groups.

Self-reported, physician-diagnosed co-morbid conditions such as allergies, chronic fatigue syndrome (CFS), fibromyalgia, and hyperprolactinemia, as well as self-reported mitral valve prolapse were much more frequently reported by women in the EA group, whereas asthma was significantly higher in the ERP cohort (Tab. III). All other co-morbid conditions were reported in similar proportions. None of the conclusions were affected by the consideration of pertinent variables, except for thyroiditis, which was statistically significantly more common in the ERP group when adjusted for calendar timing of diagnosis. However, the number of women with thyroiditis in each group was small, limiting the clinical importance of this observation.

Discussion

This study reports the first assessment of demographic, clinical, and gynecologic characteristics women with endometriosis from two geographically and ethnically different populations. Women in the EA group were slightly older, better educated, and developed symptoms they attributed to endometriosis earlier in their lives. In addition, they had higher rates of pain symptoms and fertility problems, and were more likely to have had a hysterectomy. Although higher rates of dysmenorrhea, dyspareunia, incapacitating pain, and problems getting pregnant were reported in the EA group, these symptoms were reported by the majority of patients in both populations. The higher rates of pain in the EA cohort might be related to their longer duration of endometriosis-related pain as they were younger when they first experienced symptoms, older when they answered the questionnaire, and reported longer time from onset of symptoms to diagnosis. The higher rates of problems getting pregnant reported by the EA cohort could be associated with their older age. However, it is

not surprising that women with pain symptoms were more frequently reported among the EA group, since their goal is to provide support and education to members compared to the ERP, which is registry based.

Kuohung et al (2002) reported the universality of the symptoms and demographic characteristics of endometriosis patients by studying two geographically distinct, but ethnically and culturally similar, populations (12). In contrast, our study showed that there are differences in the prevalence rates of certain symptoms and co-morbid conditions between the two populations studied, although the three cardinal symptoms of endometriosis (dysmenorrhea, dyspareunia and infertility) were common in both. The observed differences in symptom frequencies could be explained by a variety of factors unrelated to ethnicity, such as year of diagnosis, changes in practice patterns, or patient support group characteristics. We speculate that patients in the EA group may represent a population of women who actively seek support due to severity of symptoms and who also have suffered longer with symptoms associated with the disease.

Interestingly, the ERP cohort reported significantly higher rates of miscarriage than the EA group, independent of problems getting pregnant. High rates of miscarriage have also been observed when comparing women with endometriosis to the general population of women from PR, suggesting a possible association (Fourquet et al, unpublished data). Miscarriage in women with endometriosis warrants study to better understand the mechanisms at play, including a possible role of genetic factors related or unrelated to endometriosis (17).

There were differences in age at first birth between the two cohorts such that women were younger for ERP, consistent with lower proportion in the ERP reporting problems getting pregnant. However, when adjusting for this difference, the difference in problems getting pregnant remained significant. In our study, age at first birth appeared to be related to duration of endometriosis. Unfortunately, first trimester loss and chemical pregnancies may not be recognized and women responding to a survey may not report abortions. Thus, without these data we cannot speculate whether earlier pregnancy occurred or would have impacted the development of symptoms.

We observed a high prevalence of co-existing symptoms in all women diagnosed with endometriosis in both groups under study; however, the EA cohort reported higher rates. Both groups reported high rates of incapacitating pain throughout the month, and of back and leg pain. Other regional pain symptoms such as painful urination (dysuria) and diarrhea were reported by twice as many women in the EA group compared to the ERP group. Differences were also observed between the groups in systemic symptoms such as fatigue and low resistance to infections. The EA group was diagnosed over a broader and earlier time period; thus, their higher rates of hysterectomy could be due to fewer therapeutic options available in the 1950s through 1970s. The significant differences in age and other pertinent variables between the cohorts may also contribute to differences in prevalence of hysterectomy and uterine fibroids.

While similar co-morbid conditions were reported in both groups, the prevalence differed with all being higher in the EA cohort except for asthma. Other studies report that the Puerto

Rican population in the USA has the highest prevalence of asthma among all Hispanic populations, a finding ascribed to genetic factors (18). Regarding the other co-morbidities, ethnic-based differences in the prevalence and severity of allergies, and fibromyalgia, as well as in reporting pain, have been published (19–22). Thus, it is difficult to define the possible causes for the differences in rates of co-morbid conditions in this study as they may be related to genetic, geographic, ethnic or environmental factors, but may also arise because of cultural and/or geographic differences in patient diagnoses. Lack of awareness or poor education about these conditions can also lead to under reporting.

This study is limited by the fact that questionnaires differed from each other and covered two different time periods, and that each study was distinct from the other. However, when the comparisons for all symptoms, history and comorbidities were adjusted for age at diagnosis, time to diagnosis, duration of endometriosis, and calendar timing of diagnosis, there was no substantial impact on our findings. As with all studies reporting retrospective data over a prolonged time period, recall bias of endometriosis-related or co-existing symptoms is possible. The EA questionnaire did not specifically ask about diagnoses of painful bladder syndrome and irritable bowel syndrome, two other pelvic pain syndromes associated with endometriosis-associated pain; however, painful urination and diarrhea were presumed to be related to these conditions. While the education level differed between the groups, both had a large proportion of women with higher education. Regardless of these limitations, overall, this study provides valuable similarities and differences in the clinical history of two populations of patients that vary in their geographic region and ethnicity. Some selection bias may exist in each group, and results may be generalizable only to women similar to those participating in this study.

In conclusion, this study shows that endometriosis patients from two ethnically and geographically dissimilar populations vary in their reporting of symptoms associated with endometriosis and co-morbid conditions. We speculate that these two groups may be fundamentally different, not only with regards to ethnicity but also in their experience of seeking care and receiving treatment for endometriosis and related symptoms. It is also possible that cultural differences in reporting symptoms, and regional or temporal differences in treatment approaches may account for these observations. These results highlight that a universal endometriosis profile characterized by pain and infertility does exist, but that clinical scenarios and history differ, likely due to genetics, access to care, cultural issues, and years dealing with the symptoms. Therefore, the results of this study are very useful to develop hypotheses about the causes for the differences found between these two groups and conduct studies focused on each specific difference. More research is needed to better understand the factors that lead to heterogeneity in reported symptoms associated with endometriosis and their manifestations across different patient sub-groups.

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Disclosures

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TABLE I

Comparison of demographic characteristics between women with endometriosis from the United States (EA) and Puerto Rico (ERP)

Characteristics	EA N = 4,358 ^a n (%)	ERP N = 878 ^a n (%)	p-value
Diagnosis ^b			
Laparoscopy	3,753 (86.1)	765 (87.1)	0.452
Laparotomy	1,066 (24.5)	173 (19.7)	0.002
Age at survey, years ^c	36.2 ± 7.4	32.6 ± 8.3	<0.001
Education			
1 to 12 grade or High School	350 (7.8)	135 (16.2)	<0.001
Some college	889 (19.8)	272 (32.6)	
College Graduate	1,961 (43.7)	291 (34.9)	
Post-graduate	1,289 (28.7)	136 (16.3)	
Age at onset of first pelvic symptoms			
Never had symptoms	29 (0.7)	0 (0)	<0.001
<15 years	1,657 (39.9)	152 (25.0)	
15–24 years	1,719 (41.3)	254 (41.9)	
25–34 years	625 (15.0)	156 (25.7)	
35–44 years	118 (2.8)	43 (7.1)	
45+ years	10 (0.3)	2 (0.3)	

^aPercents are based on total number of women per group who responded to each question (excludes blank or non-applicable responses) and may not equal the listed denominator per group.

^bWomen may have reported both types of surgeries as a method of diagnosis; percents are based on total number per group.

^cMean ± SD.

TABLE II

Comparison of pain symptoms, gynecologic, obstetric, and other clinical characteristics between women with endometriosis from the United States (EA) and Puerto Rico (ERP)

Characteristics	EA N = 4,358 ^a n (%)	ERP N = 878 ^a n (%)	p-value ^b
Pelvic pain symptoms			
Dysmenorrhea	4,020 (98.2)	726 (83.9)	<0.001
Dyspareunia	2,810 (74.4)	418 (53.7)	<0.001
Chronic pelvic pain	4,171 (98.4)	421 (48.0)	<0.001
Pain throughout the month	2,809 (78.3)	148 (28.5)	<0.001
Incapacitating pain	3,512 (80.1)	534 (66.1)	<0.001
Gynecologic and obstetric history			
Problems getting pregnant	1,800 (69.4)	346 (53.3)	<0.001
Miscarriages	618 (14.2)	171 (20.8)	<0.001
Irregular bleeding	1,912 (49.1)	106 (20.4)	<0.001
Profuse bleeding	2,833 (70.1)	90 (17.3)	<0.001
Hysterectomy	722 (16.8)	87 (11.7)	<0.001 ^c
Uterine fibroids	866 (20.0)	149 (17.0)	0.040 ^d
Other co-existing symptoms			
Back/leg pain	3,496 (91.9)	239 (46.0)	<0.001
Abdominal pain	3,112 (85.7)	140 (26.9)	<0.001
Nausea/upset stomach	2,768 (68.8)	197 (37.9)	<0.001
Diarrhea	1,677 (56.1)	134 (25.8)	<0.001
Painful urination	1,329 (34.6)	61 (11.7)	<0.001
Low resistance to infections	1,886 (49.1)	62 (11.9)	<0.001
Low grade fever	1,404 (37.6)	13 (2.5)	<0.001
Fatigue/low energy	3,810 (91.0)	97 (18.7)	<0.001
Dizziness	2,749 (69.1)	116 (22.4)	<0.001
Chest pain	563 (21.4)	29 (4.4)	<0.001

^aPercents are based on total number of women per group who responded to each question (excludes blank or non-applicable responses) and may not equal the listed denominator per group.

^bP-values are from crude comparisons using contingency tables; in addition, all comparisons were further adjusted for pertinent covariates, such as each of age at surgical diagnosis, time to diagnosis from onset of symptoms, duration of living with endometriosis, and calendar timing of diagnosis as they were statistically significantly different between groups and may impact findings. Problems getting pregnant was also adjusted for age at time of first delivery, and hysterectomy and uterine fibroids were also adjusted for current age. Any changes in conclusions as a result of the adjustments are indicated.

^cNot statistically significant when adjusted for time to diagnosis or duration of endometriosis. As applicable due to the impact of current age, this was also not statistically significant when adjusted for age at time of completing the questionnaire.

^dNot statistically significant when adjusted for any of the covariates. As applicable due to the impact of current age, this was also not statistically significant when adjusted for age at time of completing the questionnaire.

TABLE III

Comparison of co-morbid conditions between women with endometriosis from the United States (EA) and Puerto Rico (ERP)

Conditions	EA N = 4,358 ^a n (%)	ERP N = 878 ^a n (%)	p-value ^b
Allergic conditions			
Allergies *	2,853 (65.5)	158 (23.8)	<0.001
Asthma *	631 (14.5)	122 (18.4)	0.010
Autoimmunity			
Lupus	34 (0.8)	6 (0.9)	0.646
Sjögren's syndrome	23 (0.5)	1 (0.2)	0.358
Rheumatoid arthritis	83 (1.9)	11 (1.7)	0.760
Multiple sclerosis (MS)	22 (0.5)	4 (0.6)	0.770
Endocrine disorders			
Hypoglycemia	349 (8.1)	45 (6.8)	0.279
Hyperthyroidism	66 (1.5)	5 (0.8)	0.157
Diabetes	62 (1.4)	15 (2.3)	0.126
Thyroiditis	75 (1.7)	17 (2.6)	0.161 ^c
Hyperprolactinemia *	125 (2.9)	5 (0.8)	<0.001
Hypothyroidism	290 (6.7)	32 (4.8)	0.074
Cancer			
Breast cancer	16 (0.4)	2 (0.3)	>0.999
Ovarian cancer	10 (0.2)	1 (0.2)	>0.999
Others			
Fibromyalgia *	272 (6.3)	14 (2.1)	<0.001
Mitral valve prolapse (MVP) *	636 (18.4)	37 (5.6)	<0.001
Chronic fatigue syndrome (CFS) *	197 (4.6)	7 (1.1)	<0.001

* statistically significant.

^a Percents are based on total number of women per group who responded to each question (excludes blank or non-applicable responses) and may not equal the listed denominator per group.

^b P-values are from crude comparisons using contingency tables; in addition, all comparisons were further adjusted for pertinent covariates, such as each of age at surgical diagnosis, time to diagnosis from onset of symptoms, duration of living with endometriosis, and calendar timing of diagnosis as they were statistically significantly different between groups and may impact findings. Fibromyalgia was additionally adjusted for current age when adjusting for calendar timing of diagnosis due to its differential on the observed range of calendar timing of diagnosis. Any changes in conclusions as a result of the adjustments are indicated.

^c Statistically significant ($p = 0.002$) when adjusted for calendar timing of diagnosis.