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Reproductive and Menstrual Risk Factors for Endometriosis Disease: A Case-Control Study

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Abstract

Objectives: The endometriosis prevalence in the general population is about 7%-10%. In 30% of women, endometriosis is one of the causes of primary and secondary infertility. There are various risk factors for this disease. The present study aimed to determine the reproductive and menstrual risk factors of endometriosis.

Materials and Methods: In this case-control study, 185 women of reproductive age with confirmed endometriosis were compared with 370 women of reproductive age who referred to the same center for other problems in terms of reproductive and menstruation risk factors for endometriosis. The two groups were matched for age. Data were collected using a researcher-made questionnaire based on previous studies. Finally, bivariate analysis was done by the chi-square test, and multivariate analysis was performed by the conditional logistic regression for controlling confounder variables.

Results: Based on multivariate logistic regression, early menarche age ($P=0.004$), no history of pregnancy ($P<0.001$), no child ($P=0.002$), no lactation history ($P<0.001$), high age of the first lactation ($P=0.029$), short duration of breastfeeding ($P=0.015$), no regular menstruation ($P<0.001$), short intervals between menstrual bleedings ($P=0.016$), prolonged menstruation ($P<0.001$), dysmenorrhea ($P<0.001$), dyspareunia ($P<0.001$), and recurrent vaginitis ($P<0.001$) had a significant relationship with endometriosis.

Conclusions: In general, there was a relationship between some reproductive and menstrual characteristics and endometriosis. Therefore, it seems that these characteristics can predict the occurrence of endometriosis disease.

Keywords: Case-control study, Reproductive characteristics, Menstrual characteristics, Endometriosis

Introduction

Endometriosis is a gynecologic disease that depends on estrogen (1) and is identified by the existence and implantation of the uterine endometrial stroma and glands somewhere other than their natural location (i.e., uterine endometrial cavity). The most common places in the pelvic cavity include ovaries, uterosacral ligament, and Douglas's pouch (2). Symptoms associated with this disease are menstrual pain, dyspareunia, chronic pelvic pain, irregular menstruation, or infertility (3). The prevalence of endometriosis in the general population is estimated at 7%-10% (1) although its prevalence in infertile women may be over 30% (2). The prevalence of symptoms in women suffering from pain, infertility, or both are over 35%-50% (3,4). According to a study in Iran on 441 infertile women, the prevalence of endometriosis was 18.6% based on laparoscopy findings (5). Endometriosis is often found in women of reproductive age. The average age of the diagnosis is about 25-29 years old (6). Endometriosis has complex and multifactorial etiology (7). Endometriosis develops due to factors such as hormonal changes (8) genetic changes (9), and changes in the immune system (10).

Strong evidence suggests the association between family histories and endometriosis (11). A systematic review study indicates that menarche at an early age may slightly increase the risk of endometriosis, which may be higher due to the incorrect classification of the disease in primary studies (12). The incidence rate of endometriosis in women with long-term menstrual bleeding and short intervals between menstruations is high (12,13). A cohort study showed that the risk of endometriosis in nulliparous women with early menarche and short intervals between menstrual periods is high. The high number of deliveries and the long-term lactation reduce the risk of endometriosis (14). One of the risk factors for endometriosis is age, and it usually occurs after 19-20 years of age. The genital obstructive disorder should be ruled out if endometriosis occurs before this period (15). A systematic review study suggests that oral contraceptive pills decrease the endometriosis risk by stopping ovulation and reducing the amount of bleeding in menstruation. However, the recommendation to use oral contraceptives for preventing endometriosis has not been approved (16), thus the use of intrauterine devices

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Key Messages

- Endometriosis is a disease in women of reproductive age. Etiology and pathogenesis of which aren't well defined. Therefore, further investigation to identify the risk factors of this disease seems necessary.
- Several factors including menarche age, no history of pregnancy and lactation, short duration of breastfeeding and no regular menstrual periods were associated with the possibility of endometriosis.

(copper or progesterone) does not change the progression of this disease and requires further studies (17). A review study has shown that less number of pregnancy and the first pregnancy at high ages and short-term breastfeeding lead to an increased risk of endometriosis (18). The results of a study on 1282 surgical patients in Tehran-Iran showed that gravidity, parity, family history of endometriosis, and shorter menstrual period length were associated with endometriosis (19).

Therefore, due to the importance of this disease, its reflection on the fertility of affected women, complications associated with its effects on the life of women of reproductive age, the possible association between endometriosis and some reproductive and menstrual characteristics, and the recommendation of studies for further evaluation, the present study aimed to investigate the reproductive and menstrual risk factors of endometriosis.

Materials and Methods

Study Type and Participants

This case-control study recruited women with and without endometriosis aged 20-50 years in 2017. The participants in the case group were selected from among women with endometriosis visiting Alzahra hospital over the last two years undergoing laparoscopy and open surgery with a histologic diagnosis of endometriosis and medical files in the mentioned centre. The control group was selected from among the women of reproductive age (20-50 years) visiting the same centre for other problems (e.g., vaginitis) in whom the lack of endometriosis was diagnosed by a gynaecologist based on their symptoms and considering eligibility criteria.

The inclusion criteria were age range of 20-50 years, diagnosis of endometriosis by open surgery or laparoscopy and histologic diagnosis of endometriosis or the presence of endometrioma (the case group) in addition to being married and Iranian showing willingness for participation, lacking endometriosis (control group), and having no history of tubectomy (control group), or infertility (control group).

On the other hand, the exclusion criteria included being menopausal (amenorrhea for over a year), being suspected of endometriosis or endometrioma (control group), and having endometriosis in the surgical site or the involvement of remote areas (e.g., lungs or brain). Other criteria were suffering from breast, ovarian, or endometrial cancers, having polycystic ovarian syndrome, having any life-threatening disease, and suffering from chronic pelvic pain according to woman's expression.

In this study, the sample size was determined according to the results of a pilot study on 150 participants, and then determined as $n_1 = 185$ (case group), $n_2 = 370$ (control group), and $n = 555$ (total, with the case-to-control ratio of 1:2) considering the odds ratio (OR: the odds of having sexual activity in menstrual bleeding periods in the case group compared with the control group) to be detected about 1.8.

Data Collection

The present study was confirmed by the Ethics Committee of Tabriz University of Medical Sciences (ethical code: 5/D1003687). Afterward, data collection was started in Alzahra Hospital, Tabriz, which is a referral gynaecology and midwifery hospital in Northwest Iran. By reviewing medical records, those with a confirmed histologic diagnosis of endometriosis through laparoscopy or open surgery were identified over the past two years and their addresses and telephone numbers were extracted from their records. They were contacted via telephone and briefed about research objectives and methods, and then eligibility criteria were checked, and they were requested to take part in the study. For those willing to participate, questionnaires were filled in by the researchers through interviews. After sampling in the case group, control group members were selected through purposive sampling from those visiting the gynaecology clinic of the same center for other problems (e.g., vaginitis or a medical visit) and those who did not have endometriosis as diagnosed based on symptoms by a gynaecologist colleague. Research objectives and methods were explained to them. Eligibility criteria were checked for those showing a willingness to participate, and they were recruited in case they met the criteria. Then, questionnaires were filled out through interviews with participants by the researcher. Informed consent forms were obtained from all participants, and those in the case and control groups were matched for age ±2 years.

Data Collection Tools

Data were collected by the researcher through interviews and using researcher-made questionnaires including socio-demographic characteristics and reproductive and menstruation characteristics questionnaires.

The sociodemographic characteristics questionnaire included questions on age, level of education, employment, level of income, smoking, alcohol use, and endometriosis in first-degree relatives (i.e., mother, sisters, and aunts).

The reproductive and menstruation characteristics questionnaire included questions on menarche age, age at the first sexual intercourse, pregnancy, age at the first

pregnancy, pregnancy number, number of alive children, abortion, breastfeeding, and age at the first breast feeding. The other items were related to lactation duration, use of oral contraceptives or intrauterine devices, the regularity of menstruation, menstrual cycle length and interval, dysmenorrhea, dyspareunia, ectopic pregnancy, and recurrent vaginitis.

To determine the content and face validity of the questionnaires, they were given to 10 faculty members, and corrections were applied based on their opinions.

Statistical Analysis

SPSS (version 21) was used for statistical analysis. Socio-demographic, reproductive, and menstruation characteristics were expressed using descriptive statistics such as frequency (percentage). For determining the association between sociodemographic, reproductive, and menstruation characteristics and endometriosis, the chi-square test was applied for the bivariate analysis, and conditional logistic regression was employed in the multivariate analysis to control confounding variables (i.e., the level of education, level of income, and occupation). No woman in the control group reported a history of endometrisosis in her first-degree relatives thus the family history was not included in the multivariate regression as a confounding factor. In this analysis, the OR (confidence interval) was set at 95%, and the significant level was considered $P < 0.05$.

Results

In general, 185, 370 patients with and without endometriosis were analyzed in this study. The average age of participants was 35.21 (SD = 7.09) and 35.28 (SD = 7.03) years in the case and control groups, respectively. In terms of the educational level, the percentage of university education in the case group was twice as high as in the control group. Moreover, 32 (17.3%) and 10 (2.7%) women of the case and control groups were employed, respectively. Based on the results, 13 (7%) women of the case group reported endometriosis history in their mothers and sisters, and 7 (3.8%) of them reported this record in their aunts while no woman in the control group indicated a history of endometriosis in her first-degree relatives. Only one woman in the control group had a history of smoking whereas no one in either group had a history of alcohol use (Table 1).

Based on multivariate logistic regression, the odds of endometriosis in women with a menarche ≤ 12 years was about two times higher than those who had menarche > 12 years old [OR (95% CI) = 1.90 (1.23-2.96), $P = 0.004$]. The results further revealed that 143 (77.3%) and 366 (98.9%) women in the case and control groups had a history of pregnancy, respectively, and there was a statistically significant difference between the groups [OR (95% CI) = 0.03 (0.01-0.11), $P < 0.001$]. In terms of the number of pregnancies, 102 (55.1%) and 80 (21.6%) participants in the case and control groups reported no history of pregnancy or a history of one pregnancy, respectively, and the odds of endometriosis was about four times higher than those with a history of two or more pregnancies [OR (95% CI) = 4.16 (2.74 to 6.31), $P < 0.001$].

Likewise, 125 (87.4%) women in the case group and 266 (72.9%) cases in the control group did not have any alive child or had one alive child. The odds of endometriosis was nearly 3 times higher than those with two or more alive children [OR (95% CI) = 2.16 (1.43-4.76), $P = 0.002$]. Based on the obtained data, 109 (58.9%) and 310 (83.8%) women in the case and control groups had a history of breastfeeding, respectively. The case and control groups were different in terms of the history of breastfeeding.

Table 1. Socio-demographic Characteristics of Both Case and Control Groups

Social-demographic Characteristics	Case (n = 185)	Control) n =)370
Age (y), mean (SD)	35.21 (7.09)	35.28 (7.03)
Education, No. (%)		
Illiterate/primary school	57 (30.8)	129 (34.9)
Guidance/High school, No. (%)	37 (20.0)	82 (22.2)
Diploma	39 (21.1)	107 (28.9)
University	52 (28.1)	52 (14.1)
Occupation		
Housewife	153 (82.7)	360 (97.3)
Employed	32 (17.3)	10 (2.7)
Adequacy of monthly income, No. (%)		
Inadequate	42 (22.7)	79 (21.4)
Somewhat adequate	102 (55.1)	197 (53.2)
Completely adequate	41 (22.2)	94 (25.4)
The history of endometriosis in first-degree relatives, No. (%)		
Yes	20 (10.8)	0
No	165 (89.2)	370 (100.0)

Note. SD: Standard deviation.

Only one woman in the control group had a history of smoking while no one in either group had a history of alcohol use.

In women with a history of lactation, the odds of endometriosis was lower [OR (95% CI) = 0.28 (0.18-0.44), $P < 0.001$].

The findings demonstrated that 16 (14.7%) and 80 (25.8%) participants in the case and control groups were ≤ 18 years old at the time of the first lactation, respectively. Having a lactation at a young age reduced the odds of endometriosis [OR (95% CI) = 0.50 (0.27-0.93), $P = 0.029$], and 60 (55%) and 127 (41%) participants in the case and control groups had lactation history ≤ 24 months, respectively. In women with a history of short-term breastfeeding, the chance of endometriosis was approximately 2 times higher than that of long-term breastfeeding [OR (95% CI) = 1.86 (1.12-3.08), $P = 0.015$].

Moreover, 123 (66.5%) women in the case group and 353 (95.4%) cases in the control group had regular menstruation history, and the two groups were different in terms of regular menstruation history. The chance of endometriosis was lower in women with regular menstruation [OR (95% CI) = 0.09 (0.05-0.17), $P < 0.001$]. The results indicated that 109 (58.9%) and 176 (47.6%) women in the case and control groups had a history of a menstrual interval of ≤ 28 days between menstrual periods, respectively. The chance of endometriosis was 1.5 times higher in women with a history of menstruation ≤ 28 days [OR (95% CI) = 1.58 (1.08-2.31), $P = 0.016$]. As regards the duration of menstrual bleeding, 136 (73.5%) and 357 (96.5%) women in the case and control groups had menstrual bleeding ≤ 7 days, respectively, and the chance of endometriosis was lower in women with menstruation ≤ 7 days in comparison with those who had a history of menstruation > 7 days [OR (95% CI) = 0.09 (0.05-0.19), $P < 0.001$].

Based on the results, 136 (73.5%) and 43 (11.6%) women in the case and control groups had dysmenorrhea history and the two groups differed in terms of dysmenorrhea [OR (95% CI) = 47.0 (20.5-108), $P < 0.001$]. Finally, 50 (27%) and 18 (4.9%) participants in the case and control groups had a history of recurrent vaginitis, respectively, and the chance of recurrent vaginitis in the case group was about 8 times more than the control group [OR (95% CI) = 8.49 (4.67-15.43), $P < 0.001$]. There was no statistically significant difference between the groups regarding age at the first sexual intercourse, the history of taking contraceptive pills, and the history of using intrauterine devices (Table 2).

Discussion

Endometriosis is a disease in women of reproductive age, the etiology and pathogenesis of which are not well-defined, and it is clear that there are many problems for patients, including infertility. Therefore, further

Table 2. Comparison of Reproductive and Menstrual Characteristics in Both Case and Control Groups Based on Chi-square Test and Bivariate and Multivariate Logistic Regression

Reproductive and Menstrual Characteristics	Case (n = 185) No. (%)		Control, (n = 370) No. (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age at menarche (y)					
≤12	54 (29.2)		64 (17.3)	1.97 (1.30 to 2.98)	1.90 (1.23-2.96)
>12	131 (70.8)		306 (82.7)	1	1
P value		<0.001*		<0.001	0.004
Age at first coitus (y)					
≤18	46 (24.6)		123 (33.2)	0.66 (0.44-0.98)	0.79 (0.51-1.22)
>18	139 (75.1)		247 (66.8)	1	1
P value		0.043*		0.044	0.299
Pregnancy					
Yes	143 (77.3)		366 (98.9)	0.03 (0.01-0.10)	0.03 (0.01-0.11)
No	42 (22.7)		4 (1.1)	1	1
P value		<0.001*		<0.001	<0.001
Age at first pregnancy (y)					
≤20	43 (30.1)		146 (40.0)	0.64 (0.42-0.97)	0.74 (0.47-1.17)
>20	100 (69.9)		219 (60.0)	1	1
P value		0.037*		0.038	0.208
Pregnancy number					
0.1	102 (55.1)		80 (21.6)	4.45 (3.04-6.52)	4.16 (2.74-6.31)
≥2	83 (44.9)		290 (78.4)	1	1
P value		<0.001*		< 0.001	< 0.001
Alive child number					
0 or 1	125 (87.4)		266 (72.9)	2.58 (1.49-4.45)	2.61 (1.43-4.76)
≥ 2	18 (12.6)		99 (27.1)	1	1
P value		<0.001*		< 0.001	0.002
Abortion					
Yes	51 (27.6)		122 (33.0)	0.77 (0.52-1.14)	0.76 (0.51-1.14)
No	134 (72.4)		248 (67.0)	1	1

Table 2. Continued

Reproductive and Menstrual Characteristics	Case (n = 185) No. (%)	Control, (n = 370) No. (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
P value	0.195*		0.196	0.197
Breastfeeding				
Yes	109 (58.9)	310 (83.8)	0.27 (0.18-0.41)	0.28 (0.18-0.44)
No	76 (41.1)	60 (16.2)	1	1
P value	<0.001*		< 0.001	< 0.001
Age at first lactation (y)				
≤18	16 (14.7)	80 (25.8)	0.49 (0.27-0.89)	0.50 (0.27-0.93)
> 18	93 (85.3)	230 (74.2)	1	1
P value	0.017*		0.019	0.029
Breastfeeding duration (mon)				
≤24	60 (55.0)	127 (41.0)	1.76 (1.13-2.74)	1.86 (1.12-3.08)
> 24	49 (45.0)	183 (59.0)	1	1
P value	0.011*		0.011	0.015
Using of OCP				
Yes	75 (40.5)	167 (45.1)	0.83 (0.581.19-)	1.07 (0.69-1.66)
No	110 (59.5)	203 (54.9)	1	1
P value	0.303*		0.304	0.759
Using of IUD				
Yes	42 (22.7)	120 (32.4)	0.61 (0.40-0.91)	1.08 (0.67-1.73)
No	143 (77.3)	250 (67.6)	1	1
P value	0.017*		0.018	0.765
Regular menstruation				
Yes	123 (66.5)	353 (95.4)	0.09 (0.05-0.17)	0.09 (0.05-0.17)
No	62 (33.5)	17 (4.6)	1	1
P value	< 0.001*		< 0.001	< 0.001
Cycle interval (days)				
≤28	109 (58.9)	176 (47.6)	1.58 (1.10-2.25)	1.58 (1.08-2.31)
>28	76 (41.1)	194 (52.4)	1	1
P value	0.012*		0.012	0.016
Cycle length (days)				
≤7	136 (73.5)	357 (96.5)	0.10 (0.05-0.19)	0.09 (0.05-0.19)
>7	49 (26.5)	13 (3.5)	1	1
P value	< 0.001*		< 0.001	< 0.001
Dysmenorrhea				
Yes	136 (73.5)	43 (11.6)	21.10 (13.3-33.2)	21.4 (13.2-34.8)
No	49 (26.5)	327 (88.4)	1	1
P value	< 0.001*		< 0.001	< 0.001
Dyspareunia				
Yes	82 (44.3)	7 (1.9)	41.28 (18.5-92.0)	47.0 (20.5-108.0)
No	103 (55.7)	363 (98.1)	1	1
P value	< 0.001*		< 0.001	< 0.001
Ectopic pregnancy				
Yes	7 (3.8)	5 (1.4)	2.87 (0.89-9.17)	
No	178 (96.2)	365 (98.6)	1	
P value	0.116*		0.075	
Recurrent vaginitis				
Yes	50 (27.0)	18 (4.9)	7.24 (4.07-12.86)	8.49 (4.67-15.43)
No	135 (73.0)	352 (95.1)	1	1
P value	< 0.001*		< 0.001	< 0.001

Abbreviations: OCP: Oral contraceptive pills; IUD: Intrauterine device; OR, Odds ratio.

* Chi-square test.

Note. Conditional logistic regression was employed in the multivariate analysis to control confounding variables such as the level of education, level of income, and occupation. The history of ectopic pregnancy was not introduced into the multivariate logistic regression model due to low numbers

investigation to identify the risk factors of this disease seems necessary. It is believed that there is an association between some reproductive and menstrual characteristics and endometriosis. Based on the results of multivariate regression, several parameters were associated with the possibility of endometriosis. These factors included the early menarche age, no history of pregnancy, no child, no lactation history, high age at the first lactation, short duration of breastfeeding, no regular menstrual periods, short interval between menstrual bleedings, and prolonged menstrual bleeding. The case group reported a history of dysmenorrhea and dyspareunia and recurrent vaginitis more than the control group.

Parasar et al reviewed the epidemiology and risk factors of endometriosis and studied biomarkers for the early and non-invasive diagnosis of this disease. Based on their results, early menarche, short intervals between menstruation, and height were related to a great risk of endometriosis while the number of parity, a high body mass index (BMI), and smoking were associated with a low risk of this disease (20).

The results of case-control research conducted by Meaddough et al in the United States showed that the mean age of menarche was not statistically significant between endometriosis patients (the case group) and health individuals (the control group). The case group reported menstrual bleeding of more than 7 days and the interval between menstrual periods of less than 24 days. In contrast, menstrual periods with 24-28, 29-32, and more than 32 days were less in the case group compared with the control group, representing a significant difference between the two groups (13).

In another research, Heilier et al investigated individual and environmental risk factors associated with endometriosis and found that there was an inverse relationship between high parity and endometriosis. Lactation status, menarche age, length of menstrual periods, and the amount of bleeding were similar among the groups. The case group often reported dysmenorrhea and dyspareunia more than the control group. The duration of contraceptive pill use in patients with endometriosis was less compared to women without endometriosis. There was no association between smoking and disease. Women with deep endometriosis demonstrated more alcohol consumption in comparison with those with endometriosis (21).

In a case-control study by Moini et al in Iran, the case group was categorized into two subgroups according to disease stages, namely, stages one and two (mild endometriosis), as well as three and four (severe endometriosis). The results revealed a significant difference between the group (two case groups and one control group) in terms of age, duration of infertility, BMI, dyspareunia, dysmenorrhea, and family history (22). In their systematic review, Nnoaham et al assessed the association between menarche age and the risk of endometriosis and concluded that early menarche slightly increased the endometriosis risk, which could be higher than this due to the weakness of the studies (12).

Missmer et al investigated reproductive history and endometriosis for 10 years on women aged 25-42 years and showed that participants with early menarche age and a short interval between menstrual periods had the highest risk for disease. The number of parity and the length of lactation in women were related to a decreased risk of endometriosis (14). The results of a review study by Grandi et al in Italy represented that the low number of pregnancies and high age in the first pregnancy and short-term lactation led to an increase in the risk of endometriosis (18). In another study by Gemmill et al, women with endometriosis reported recurrent vaginitis more than those without endometriosis (23).

The result of research by Chaichian et al indicated no significant difference in terms of age, education level, breastfeeding, infertility duration, and menstrual flow. However, endometriosis patients had longer durations of marriage, older age at first pregnancy, a lower BMI, a shorter interval of menses, and a history of irregular menstrual cycles compared to the women without endometriosis. According to Chaichian et al study(5), the increased number of pregnancies significantly reduces the risk of endometriosis.

Ashrafi et al demonstrated that gravidity, parity, family history of endometriosis, and shorter durations of the menstrual cycle had a significant relationship with endometriosis while the length of menstrual bleeding and menarche age were not correlated with the risk of endometriosis (19).

The results of this study are consistent with those of all the above-mentioned studies in terms of the association between menarche age and endometriosis except for studies by Heilier et al (21), Meaddough et al (13) Ashrafi et al (19), and Moini et al (22), in which two case and control groups had no significant difference with regard to the average age of menarche. In the study by Heilier et al, the groups were matched in terms of the BMI. In the study by Meaddough et al, the sample size was much higher than that of the present study, thus these factors may be the cause of such differences. There was a significant difference between the groups in terms of the first pregnancy age, the number of pregnancies, the history of breastfeeding, and the duration of lactation. The findings of this study are in line with the results of Missmer et al (14), Heilier (21) et al, Parasar et al (20), and Grandi et al (18).

As regards the association between short menstrual periods and long-term menstrual bleeding with endometriosis, the results of all of the aforementioned studies corroborate with the findings of this study except for the findings of the study by Heilier et al (21), indicating that the duration of the menstrual period and menstrual bleeding was similar between the groups. This difference

was probably due to the sample size of the present study and that of the study by Heilier et al. In the study by Heilier et al, dysmenorrhea and dyspareunia were reported more repeatedly in endometriosis patients compared to those without endometriosis, which matches the result of this study. The findings of a systematic review by Vercellini et al (16) indicated that the use of oral contraceptive pills with stopping in ovulation and the reduction in menstrual bleeding may reduce the risk of endometriosis, but it was not approved to take oral contraceptive pills for the primary prevention of endometriosis. Additionally, in the study by Heilier et al (21), participants with endometriosis had a shorter duration of contraceptive pill use in comparison with the control group. However, the two groups in this study had no significant difference in the history of contraceptive use.

The findings of a study by McLeod and Retzloff (17) showed that the use of intrauterine devices (copper or progesterone) had no significant impact on the progression of endometriosis and recommended further studies in this respect. Moreover, the two groups in the present study had no significant difference in terms of the use of intrauterine devices (copper or progesterone). Regarding the history of recurrent vaginitis, the findings of this study are in conformity with those of Gemmill et al (23) although more studies are necessary in this regard.

Although there are differences among different studies, it seems that the association between endometriosis and some indicators of reproductive and menstrual characteristics are unavoidable, because factors such as pregnancy and lactation can reduce the chance of implantation of endometrial tissue by stopping ovulation, or the short interval between menstrual periods and prolonged menstrual bleeding can be associated with the possibility of reversal menstrual bleeding and the hypothesis of retrograde menstruation as the main pathogenesis of this disease; however, further studies are considered necessary.

In this study, patients with endometriosis were selected based on a definite histological diagnosis by laparoscopy and women without endometriosis were selected based on symptoms, the inclusion and exclusion criteria, along with the approval of the absence of endometriosis by a gynecologist. The questionnaires were completed by a constant interviewer for both groups. Furthermore, it was attempted to control all the confounding factors. For this purpose, the two groups were matched in terms of age, and all possible confounding factors in the statistical analysis were controlled.

The criterion for the definite diagnosis of endometriosis was histological diagnosis by laparoscopy or laparotomy. However, one of the limitations of the present study was that the participants of the control group were only diagnosed based on symptoms by a gynaecologist. Thus, future studies may choose to select case and control groups from among women in whom the presence or the lack of endometriosis was confirmed by laparoscopy or laparotomy. Accordingly, further studies are recommended on this topic.

Conclusions

Based on the results of this study, there was a relationship between some reproductive and menstrual characteristics and endometriosis. Therefore, the presence of these risk factors can help in early identifying and treating endometriosis, and consequently, it can prevent complications due to this disease. According to the findings and considering the multiple complications of the disease, including pelvic pain and infertility, it seems logical to recommend that healthcare teams educate women of reproductive age about early pregnancy and lactation while avoiding delayed pregnancy at high ages due to subsequent complications. Eventually, attention to endometriosis symptoms and referral to a physician for the early diagnosis of the disease are recommended to prevent its progress.

Authors' Contribution

SM involved in the conception and design, acquisition of data and drafting the manuscript. MM and NA involved in the conception and design, acquisition of data, analysis of the data, interpretation of data and writing this manuscript. MK, BSO and MJS involved in the conception and design, interpretation of the data and revising this manuscript. All authors gave their final approval of this version to be published.

Conflict of Interests

None declared.

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