Effects of Endometriosis on Sleep Quality of Women: Does Life Style Factor Make a Difference?

Samaneh Youseflu
Tarbiat Modares University Faculty of Medical Sciences

Shahideh Jahanian Sadatmahalleh (shahideh.jahanian@modares.ac.ir)
Tarbiat Modares University Faculty of Medical Sciences

Ghazall Roshanzadeh
Tarbiat Modares University Faculty of Medical Sciences

Azadeh Mottaghi
Tehran University of Medical Sciences

Anoshirvan Kazemnejad
Tarbiat Modares University Faculty of Medical Sciences

Ashraf Moini
Tehran University of Medical Sciences

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Abstract

Background This study aimed to evaluate the impact of lifestyle factors, and sleep quality on endometriosis risk. Methods Of the 156 infertile women approached for the study, 78 women had endometriosis and 78 were included in the control group. At first, each participant completed a checklist including questions about demographics, physical activity, reproductive and menstrual status. Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI). Dietary data were collected using a validated 147-item semi-quantitative FFQ. Results Irregular menstrual status, menorrhagia, dysmenorrhea, pelvic pain, history of abortion, family history of endometriosis were associated with endometriosis risk (P <0.05). In women with physical activity more than 3 hours per week, high consumption of the dairy product, and fruit endometriosis is less common (P <0.05). The total PSQI score, and the scores for subjective sleep quality, sleep latency, sleep disturbance domains were significantly different between the two groups (P <0.05). In women with endometriosis, poor sleep quality was associated with dysmenorrhea, pelvic pain, dyspareunia, physical activity, and consumption of the dairy product, fruit, and nut (p<0.05). Conclusion In endometriosis women, sleep quality was lower than healthy individuals. Lifestyle factors can effect on sleep quality of these patients.

Background

Endometriosis is the benign proliferation of functioning endometrial glands and stroma in ectopic locations outside the uterine cavity (1), which affects an estimated approximately 10.8 per 1000 of reproductive age women (2). A high prevalence of dysmenorrhea, dyspareunia, non-cyclic pelvic pain, infertility and menstrual disorders (such as menorrhagia, menorrhagia, spotting) has been seen in these patients (1, 3). Although the exact pathophysiology of this disease is not clear, it is believed agents that impress the volume of retrograde menstruation or affect woman's aptitude for implantation of the endometriotic lesion are involved in the appearance and progression of endometriosis(4). Some of the studies introduced that the appearance of endometriosis has been developed by hormonal and immunological mechanisms, genetic and inflammatory processes, as well as environmental and lifestyle factors (5).

Lifestyle factors play an important role in preventing many chronic diseases. Available evidence on the effect of lifestyle-related factors such as physical activity, nutritional status, body mass index, smoking, and SQ on endometriosis is controversial (1, 6–9). Therefore, modified lifestyle recommendations in these patients have been discussed. For example, some studies depicted the anti-estrogenic activity of cigarette has a protective effect on endometriosis, others suggested that cigarette with an impact on pro-inflammatory gene overexpression can trigger inflammation (6, 7).

Sleep is an essential physiological process that can be impressed by many medical and sleep disorders. Several studies have demonstrated that sleep disorder is a common symptom in women with endometriosis (10, 11). Recently, a relationship between endometriosis-related symptoms such as pain and sleep disorder has been reported (12). Sleep disorder and changes in the melatonin level can be a
diverse effect on the reproductive system (13, 14). There is compelling evidence to implicate that endogenous melatonin acts as an important analgesic, sleep inducer and regulator of the circadian rhythm, antioxidant, anticarcinogenic, immunoregulator, and anti-inflammatory agent (13, 14).

The purpose of the current study was to evaluate the impact of lifestyle factors including physical activity levels, diet, BMI, cigarette smoking, and SQ on endometriosis risk. Also in this essay, the impact of food intake, socio-demographic and clinical characteristics on sleep disorder of women with endometriosis were determined.

Methods

The study was conducted as a case-control study survey between May 2016 and February 2017 on 156 infertile women (78 women with endometriosis and 78 healthy women) that attending in Infertility Clinic of Arash Hospital in Tehran, Iran.

Based on the laparoscopy results, those women with abnormalities other than endometriosis were excluded from the study. Participants were divided into two groups: a case group, including 78 women with pelvic endometriosis, and a control group consisting of 78 women with a normal pelvis. Eligibility criteria for inclusion in the study were including age between 18–45 years, absence of the history of chronic diseases or mental disorder according to self-report of women, Iranian race, Non-occurrence of stressful events in the 12 months ago.

Ethical approval for the study was obtained from the Regional Ethics Committee at Tarbiat Modares University of Medical Sciences (IR.TMU.REC.1395.358). All women voluntarily participated and signed informed consent.

During the first visit, the weight and height of all women recoursing to the infertility clinic are measured. Body Mass Index (BMI) is calculated as weight divided by height squared (kg/m²).

A socio-demographic questionnaire including questions about socio-economic status (such as age, educational level, occupational status, income, and smoking history) was completed. The following, questions were asked about menstrual and reproductive characteristics (such as menstrual pattern, cycle regularity, menstrual duration, amount of menstrual bleeding, length of the menstrual cycle, premenstrual spotting, menarche age, presence of dysmenorrhea, dyspareunia and chronic pelvic pain, gravidity, parity, history of using contraception).

Participants were asked to report their exercise times/week. Based on their response, the participants' physical activity was determined at three levels: first level: low physical activity (less than one hour per week), second-level: moderate physical activity (2–3 hours per week), and third-level: high physical activity (more than 3 hours per week).

A semi-quantitative 147-item FFQ was applied to obtain dietary information. This questionnaire included a list of dietary items (with standard serving measures) commonly consumed by Iranians. The Persian
version of FFQ has previously been evaluated for both reliability and validity (15). The participants were asked to report their usual food intake during the previous year on a daily, weekly, monthly and yearly basis; all these were converted to daily intakes. Portion sizes of the consumed food were transformed to grams by using domestic measurement.

All consumed food items were analyzed for their energy and nutrient components by a nutrient database (Nutritionist 4, Mosby Nutritract software, and ver.7.0, N-Squared Computing, Salem, OR, USA).

For assessment of dietary sources of melatonin, we considered food rich of tryptophan including dairy product, nut (peanut, almond, pistachio, and walnuts), fruit (banana, apple, kiwi, peach, and strawberry, orange) and meat (red meat, pultatory, and fish).

Multiple aspects of SQ during the previous month were assessed using the valid and reliable Persian version of the Pittsburgh Sleep Quality Index (PSQI) (16). This questionnaire contains 19 items in seven categories (sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction) on a scale from 0 to 3; so the total score of PSQI is from 0 to 21. A total score higher than 5 identifies poor SQ and scores lower than 5 show the absence of sleep disorder.

Statistical analysis was performed using Statistical Package for Social Science (version 21). To check the variables’ normality, Kolmogorov–Smirnoff’s (KS) test was run. Comparisons between two groups were done using Independent Samples T-Test, Mann-Whitney’s test (MW), Chi-square tests, and logistic regression model.

**Results**

Considering general risk factors, menstrual status (OR: 2.80; %95CI: 1.23–4.38; P = 0.01), menorrhagia (OR: 2.98; %95CI: 1.31–3.76; P = 0.007), dysmenorrhea, (OR: 4.61; %95CI: 3.31–5.18; P < 0.001) pelvic pain, (OR: 15.31; %95CI: 12.95–17.43; P < 0.001) history of abortion (OR: 2.36; %95CI: 1.05–3.28; P = 0.04), Family history of endometriosis (OR: 4.05; %95CI: 2.08–7.14; P = 0.04), and physical activity more than 3 hours per week (OR: 0.3; %95CI: 0.13–0.65; P = 0.04), were associated with endometriosis risk. There was no significant relationship between, age, age at menarche, educational level, OCP use, BMI, smoking and endometriosis risk (P > 0.05) (Table 1).

Table 2 indicates that the intake of dairy products and fruit rich in tryptophan in women with endometriosis is less than the control group (P = 0.02). Consumption of other food groups such as vegetables, meat, nut, fast food, and processed snacks was no significant difference between two groups (P > 0.05). The total PSQI score (P < 0.001) and the scores for the subjective sleep quality (P = 0.002), sleep latency (P < 0.001), sleep disturbance (P < 0.001) domains were significantly different between women with and without endometriosis.
Table 3 shows poor SQ was statistically significantly associated with dysmenorrhea ($p = 0.03$), pelvic pain ($p = 0.02$), dyspareunia ($p = 0.04$), physical activity ($p < 0.001$), and consumption of dairy product ($p = 0.03$), fruit ($p = 0.03$), and nut ($p = 0.02$).

**Discussion**

The current study was designed to compare the SQ of women with and without endometriosis and determine the relationship between lifestyle factors and SQ in women with endometriosis. SQ as an important factor on women's physical and mental health can change by many condition. The main finding of the current study showed that endometriosis has a negative impact on women's SQ. Our results also showed that scores of subjective sleep quality, sleep latency and sleep disturbance subscales were significantly less in patients than healthy women.

In consistence with our results, Leone et al.'s study showed that a high prevalence of poor SQ, daytime sleepiness, sub threshold insomnia, and moderate clinical insomnia was seen in women with endometriosis (12). Another study demonstrated that night Shift job, especially working more than half of the shifts on a work at night, and Sleep Pattern Change on days off were associated with endometriosis risk (17). The result of one clinical trial demonstrates, in women with endometriosis, treatment with melatonin (10 mg for 8 week) compared with placebo reduced daily pain, dysmenorrhea, dysuria, and dyschezia. Also improved SQ, reduced using an analgesic and brain-derived neurotropic factor (BDNF) level (18).

Our finding reveal that in these patient some lifestyle factors such as exercise, diet and clinical symptoms can modify this relationship. For example, a better SQ was seen in women with endometriosis who had a diet rich in dairy products, nut, and fruits. Dairy products and some fruit (banana, kiwi, apple, peach, strawberry, and orange) are sources of tryptophan. For melatonin production, tryptophan is converted to serotonin then to N-acetyl serotonin, and finally to MLT (19). Melatonin can regulate inflammation and immune function and protect against oxidative stress, therefore, in this way can reduce the risk of endometriosis (20). Melatonin can also improve SQ in these women (18).

Diet also considered as a main risk factor of endometriosis. Between dietary items, only consumption of the dairy product and fruit (including banana, kiwi, apple, peach, strawberry, and orange) were different between women with and without endometriosis. some studies confirmed our results (21, 22).

Regarding the results, women with endometriosis were more likely to experience an increase in abnormal menstrual status, menorrhagia, dysmenorrhea, pelvic pain, abortion when compared with healthy women. Clinical symptoms of endometriosis such as pain and menorrhagia can worse women's SQ. Loring et al. study demonstrated that increased deep sleep onset latency is associated with poor SQ, and besides, poor SQ leads to greater pain sensitivity the next day (10).
Our finding suggest that high levels of physical activity are associated with reduced risk of endometriosis. Regular physical exercise could be to improve levels of immune and anti-inflammatory markers and reduced menstrual flow that could lead to decreased endometriosis risk (8). On the other hand, in women with a higher level of exercise, increased levels of sex hormone-binding globulin (SHBG) can lead to reducing the level of bioavailable estrogen (8). Insulin resistance and hyperinsulinemia have been related to endometriosis risk that physical activity can reduce these. In the result of one meta-analysis that integrated the results of nine studies, physical activity may reduce endometriosis risk, although this relationship was not statistically significant (8).

We also found that exercise is a main modifier that can improve SQ of women with endometriosis. Regular exercise can enhance melatonin secretion and in this way improve the SQ of patients with insomnia (23).

Recently, several studies were conducted on the influence of endometriosis on SQ. To our knowledge, this survey is the first research which assessed the role of life style factors on SQ of women with endometriosis. The use of validated questionnaires (eg, FFQ, and PSQI), and confirmed diagnosis through laparoscopy are other strengths of this study.

Despite the strengths of this study, the results have some limitations: First, the evaluation of physical activity was based on self-report and we don't use validate the questionnaire, therefore, it may be affected by results. Second, like other case-control studies, selection and recall bias is a concern.

**Conclusion**

Lifestyle factor such as diet and physical activity have a major impact on endometriosis risk. In women with endometriosis, SQ was lower than healthy individuals. Fruit, dairy, and nut consumption, and exercise can effect on SQ of endometriosis women. Therefore, counseling about diet and physical exercise in these women is recommended.

**Abbreviations**

FFQ
Food Frequency Questionnaire
PSQI
Pittsburgh Sleep Quality Index
SQ
Sleep Quality
SHBG
Sex Hormone-binding Globulin
MLT
Melatonin
Declarations

Ethics approval and consent to participate

The study was approved by the Tarbiat Modares University of Medical Sciences (IR.TMU.REC.1396.659). All procedures were in accordance with the ethical standards of the Regional research committee and with the Declaration of Helsinki 1964 and it later amendments. Informed consent was obtained from all participants included in the current study.

Consent for publication

All the women were informed about the aims of the project, and gave a written consent before participating in the study.

Availability of data and materials

The data sets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflict of interest.

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Authors’ contributions

SH.J, A.K, A.M, S.Y contributed to the conception and design of the study; SY, and GH.R did the literature search; S.Y and GH.R contributed to data collection; A.K performed the statistical analysis; SY, A.M, A.M and SH.J wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Tables

Table 1. Demographic and lifestyle characteristics of Endometriosis cases and control women.
| Characteristics | Case (78) | Control (77) | p-value | OR       |
|----------------|-----------|--------------|---------|----------|
| Age            | 31.01±6.55| 29.35±6.99   | 0.13    | 1.03(0.99-1.09) |
| Age at menarche|           |              |         |          |
| Less than 11 year | 8(10.26)  | 9(11.69)     | 0.77    | 0.86(0.31-2.37) |
| More than 12 years | 70(89.74) | 68(87.18)    | 1.00*   |          |
| Education      |           |              |         |          |
| Universitically | 42(53.85) | 38(49.35)     | 0.58    | 0.83(0.44-1.57) |
| Non Universitically | 36(46.15) | 39(50.65)    | 1.00*   |          |
| BMI            | 23.64±4.11| 23.69±3.58   | 0.93    | 0.99(0.92-1.08) |
| OCP use        |           |              |         |          |
| Yes            | 10(13.16) | 12(15.58)    | 0.67    | 0.82(0.33-1.03) |
| No             | 66(86.84) | 65(84.42)    | 1.00*   |          |
| Breast feeding history | | | | |
| Bottle feeding | 8(11.94)  | 5(6.49)      | 0.37    | 1.69(0.53-2.43) |
| Breast feeding | 68(89.47) | 72(93.51)    | 1.00*   |          |
| Family history |           |              |         |          |
| Yes            | 11(14.10) | 3(3.90)      | 0.04    | 4.05(2.08-7.14) |
| No             | 67(85.90) | 74(96.19)    | 1.00*   |          |
| Abortion       |           |              |         |          |
| Yes            | 22(28.20) | 11(14.29)    | 0.04    | 2.36(1.05-3.28) |
| No             | 56(71.79) | 66(85.71)    | 1.00*   |          |
| Menstrual status |         |              |         |          |
| Regular        | 55(71.43) | 67(87.01)    | 0.01    | 1.00*    |
| Irregular      | 23(29.49) | 10(12.99)    | 2.80    | (1.23-4.38) |
| Menorrhagia    |           |              |         |          |
| Yes            | 24(30.77) | 10(12.99)    | 0.007   | 2.98(1.31-3.76) |
| No             | 54(69.23) | 67(87.01)    | 1.00*   |          |
| Dysmenorrhea   |           |              | <0.001  | 4.61(3.31-5.18) |
| Yes            | 59(75.64) | 31(40.26)    |         |          |
| No             | 19(24.36) | 46(59.74)    | 1.00*   |          |
| Pelvic pain    |           |              | <0.001  | 15.31(12.95-17.43) |
| Yes            | 44(56.41) | 6(7.79)      |         |          |
| No             | 34(43.59) | 71(92.21)    | 1.00*   |          |
| BMI            | 23.64±4.11| 23.69±3.58   | 0.93    | 0.99(0.92-1.08) |
| Abortion       |           |              |         |          |
| Yes            | 22(28.20) | 11(14.29)    | 0.04    | 2.36(1.05-3.28) |
| No             | 56(71.79) | 66(85.71)    | 1.00*   |          |
| Physical activity |         |              |         |          |
| Less than 1 hours per week | 41(52.56) | 26(33.77)    | 1.00*   |          |
| 2-3 per week   | 22(28.20) | 19(24.67)    | 0.008   | 0.73(0.33-1.61) |
| More than 3 hours per week | 15(19.23) | 32(41.56)    | 0.30     | (0.13-0.65) |
| Smoking        |           |              |         |          |
| Yes            | 6(7.69)   | 3(3.90)      | 0.31    | 2.06(0.49-3.53) |
| No             | 72(92.31) | 74(96.10)    | 1.00*   |          |

Data are demonstrated as n (%) or mean ± SD.

*Reference category, OR; Odds ratio, CI; Confidence interval, BMI; Body mass index, OCP; Oral contraceptives.
Table 2: Comparison of sleep quality, and food intake between women with and without endometriosis.

|                          | Case (N=78) mean ± SD | Control (N=77) mean ± SD | p-value |
|--------------------------|------------------------|--------------------------|---------|
| Obstructive sleep quality| 1.35±0.82              | 0.97±0.74                | 0.002   |
| Ep latency               | 1.60±1.07              | 0.96±0.95                | <0.001  |
| Station of sleep         | 0.36±0.68              | 0.32±0.76                | 0.324   |
| Time function            | 0.97±1.01              | 0.79±0.81                | 0.383   |
| Ep disturbance           | 1.38±0.63              | 0.83±0.54                | <0.001  |
| Ep efficiency            | 0.47±0.77              | 0.33±0.78                | 0.07    |
| Ep medication            | 0.33±0.81              | 0.23±0.58                | 0.844   |
| Ul score                 | 6.47±3.34              | 4.45±3.26                | <0.001  |

Item food intake

| Item                  | Case (N=78) mean ± SD | Control (N=77) mean ± SD | p-value |
|-----------------------|------------------------|--------------------------|---------|
| Banana                | 19.72±17.82            | 24.65±21.19              | 0.12    |
| Peach                 | 21.55±19.30            | 26.72±23.14              | 0.218   |
| Strawberry            | 0.61±0.71              | 0.83±1.69                | 0.31    |
| Kiwi                  | 15.84±17.59            | 22.85±23.58              | 0.10    |
| Orange                | 38.80±28.01            | 51.26±39.58              | 0.128   |
| Apple                 | 39.56±34.13            | 44.22±32.18              | 0.28    |
| sum                   | 151.33±78.31           | 188.93±94.96             | 0.008   |
| Milk                  | 98.19±104              | 135.45±17.63             | 0.03    |
| Cheese                | 19.23±17.53            | 17.14±13.54              | 0.6     |
| Yoghurt               | 135.74±107.04          | 187.13±150.78            | 0.03    |
| Total dairy product   | 317.30±182.18          | 401.91±217.65            | 0.02    |
| Peanut                | 0.29±0.57              | 0.28±0.49                | 0.64    |
| Pistachio             | 0.63±0.99              | 0.85±1.33                | 0.45    |
| Almonds               | 2.20±3.02              | 2.35±2.46                | 0.46    |
| Almond                | 0.72±1.24              | 0.66±1.41                | 0.23    |
| Total nuts            | 3.85±4.59              | 4.15±4.17                | 0.61    |

Item food intake

| Item                  | Case (N=78) mean ± SD | Control (N=77) mean ± SD | p-value |
|-----------------------|------------------------|--------------------------|---------|
| Poultry               | 28.38±18.16            | 26.81±18.75              | 0.49    |
| Fish                  | 9.35±8.33              | 12.65±13.44              | 0.15    |
| Red meat              | 20.76±17.58            | 25.77±19.70              | 0.07    |
| Processed snacks      | 12.37±16.09            | 8.87±9.41                | 0.26    |
| Processed snacks      | 12.17±17.57            | 9.61±9.72                | 0.37    |

Table 3. Quality of sleep among endometriosis women by socio-demographic, clinical characteristics and food intake.
| Variable                     | Good sleeper (PSQI ≥ 5) (N=31) | Poor sleeper (PSQI < 5) (N=47) | p-value |
|------------------------------|---------------------------------|--------------------------------|---------|
| Age                         | 31±7.02                         | 31.02±6.31                     | 0.99    |
| Education                   |                                 |                                |         |
| University                  | 17(54.84)                       | 19(40.42)                      | 0.21    |
| Non university              | 14(45.16)                       | 28(59.57)                      |         |
| MI                          | 23.13±3.20                      | 23.98±4.61                     | 0.37    |
| Menstrual cycle             |                                 |                                |         |
| Regular                     | 26(83.87)                       | 39(82.98)                      | 0.92    |
| Irregular                   | 5(16.13)                        | 8(17.02)                       |         |
| Menorrhagia                 |                                 |                                |         |
| Yes                         | 9(29.03)                        | 15(31.91)                      | 0.79    |
| No                          | 22(70.97)                       | 32(68.08)                      |         |
| Dysmenorrhea                |                                 |                                |         |
| Yes                         | 20(64.52)                       | 40(85.11)                      | 0.03    |
| No                          | 11(35.48)                       | 7(14.89)                       |         |
| Vaginism                    |                                 |                                |         |
| Yes                         | 11(35.48)                       | 28(59.57)                      | 0.04    |
| No                          | 20(64.52)                       | 19(40.43)                      |         |
| Pelvic pain                 |                                 |                                |         |
| Yes                         | 12(38.71)                       | 31(65.96)                      | 0.02    |
| No                          | 19(61.29)                       | 16(34.04)                      |         |
| Physical activity           |                                 |                                |         |
| Less than 1 hour            | 9(29.03)                        | 33(70.21)                      | <0.001  |
| Between 2-3 hours           | 10(32.26)                       | 11(23.40)                      |         |
| More than 3 hours           | 12(38.71)                       | 3(6.38)                        |         |
| Diet                        |                                 |                                |         |
| Dairy product               | 375.56±157.67                   | 278.88±188.53                  | 0.02    |
| Red Meat                    | 18.90±16.32                     | 21.98±18.75                    | 0.47    |
| Fish                        | 8.37±8.39                       | 9.99±8.32                      | 0.32    |
| Pultatory                   | 28.27±17.38                     | 28.45±18.84                    | 0.92    |
| Nut                         | 6.14±7.49                       | 2.93±2.99                      | 0.01    |
| Fruit                       | 227.23±68.94                    | 244±75.70                      | 0.03    |