

# Sexual Activity during Menstruation as A Risk Factor for Endometriosis: A Systematic Review and Meta-Analysis

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## Abstract

Up to now, limited studies have been done to evaluate the effect of sexual activity during menstruation on the endometriosis. However, due to the menstrual-related symptoms of endometriosis, this study aimed to systematically review the published articles on the association between sexual activity through menstruation and endometriosis. This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). This study examined all published observational studies on the association between sexual activity during menstruation and endometriosis, on the basis of the PICOS from conception until September 2021. The Newcastle-Ottawa Quality Assessment Scale was used to evaluate the quality of the articles. Also, Meta-analysis was conducted using Review Manager (RevMan 5.3). Out of the 1,905 retrieved articles of related databases, four studies comprised a total of 3641 patients (2251 cases and 1390 controls), which fulfilled the inclusion criteria, and equally encompassed high (2/4) and low (2/4) methodological quality, were reviewed. The results of all pooled studies showed that the probability of having sexual activity during menstruation is approximately two times higher in the women with endometriosis compared to women without endometriosis [odds ratio (OR)=1.80, 95% confidence interval (CI): 1.12 to 2.90, P=0.02, I<sup>2</sup>=78%, Tau=0.17, Chi<sup>2</sup>=13.72, P=0.003]. In this review, the sexual activity during menstruation was found to be an influencing factor for endometriosis. Due to the importance and complexity of endometriosis and the dearth of evidence on this topic, further studies with more robust designs are recommended.

**Keywords:** Endometriosis, Menstruation, Meta-Analysis, Sexual Activity, Systematic Review

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## Introduction

Endometriosis is a prolonged, benign and progressive inflammatory gynecological disease. It is defined as the existence of endometrial tissue outside the uterine cavity (1, 2). The pelvic cavity was the most frequent site of endometriosis lesions may involve the uterosacral ligament, ovaries, and Douglas' pouch (3). Approximately ten percent of women of the reproductive age (176 million) are affected by endometriosis worldwide (4-7). It is associated with a number of symptoms that can be disturbing for patients and affect their quality of life (8, 9). The prevalence of endometriosis in symptomatic women estimates up to 75% (10-12). The laparoscopy findings of a study conducted on the 441 infertile Iranian women indicated that the prevalence of endometriosis was about 18.6% (10). Endometriosis is often labeled "the missed disease" (13). Endometriosis may be existent for a long time before it is detected (14). The ordinary age of the diagnosis is about 25-29 years old, while the overall delay in diagnosis, especially in European countries, is about 5-10 years (15, 16).

It is noteworthy that the etiology and pathogenesis of endometriosis are poorly understood (17). It develops due to factors such as hormonal imbalances (11) genetic alteration, and changes in the immune system (18-20).

Lack of established theory of endometriosis expressions of the retrograde menstruation is generally accepted to define the spread of endometrial soft tissue to the peritoneal cavity during the open fallopian tubes during menstruation (17, 18). In this way, studies on the uterine pressure during menstruation revealed that the contraction of the fallopian tubes and myometrium considerably increases during ovulation and menstruation (21). It supposes that the volume and level of retrograde menstruation play an essential role in the emergence and progress development and severity of the endometriosis (22). There is a hypothesis that sexual activity during menstruation can surge retrograde menstruation, planting tissue of endometrium elsewhere, and thus elevating risk of endometriosis (23). According to the results of studies

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that have considered the relationship between sexual activity during menstruation and endometriosis; endometriosis in women who had sexual intercourse during menstruation, was higher in comparison with whom abstinence from sexual intercourse in the same time (23-25). The results of another study showed that sexual activity during menstruation was lower in women with endometriosis compared to women without endometriosis (26). Although, limited studies have been performed to assess the effect of sexual activity during menstruation on the endometriosis, there are important issues that must not be neglected such as quality of life of women of reproductive age (13, 16, 27, 28), and fertility of affected women. The present systematic review and meta-analysis aimed to answer to the question of whether sexual activity during menstruation can be related to the occurrence of endometriosis.

## Materials and Methods

### Identification and selection of articles

This review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. It was limited to the published research articles that compared sexual activity during menstruation in women with and without endometriosis. The Participant, Intervention, Control group, Outcome (PICO) model was used as a search tool in which; i. Participants: women with confirmed endometriosis diagnosis, ii. Interventions: none, iii. Control group: women without endometriosis, iv. Outcome: endometriosis affected women. Two members of our team checked all published studies, national and international databases, including Medline (via PubMed), Web of Science, Scopus, and ProQuest as well as Persian databases consisting of SID, Magiran, Iranmedex. Also, they restricted their search to English and Persian languages until September 21<sup>st</sup>, 2021. Finally, the reference list of retrieved studies was manually searched to find further relevant studies. We excluded the Grey literature, that did not pass the peer-reviewed process and also, not available at the time of this analysis. These included abstracts, conferences, proceedings, presentations, unpublished data, regulatory data, government publications, dissertations/theses, reports, patents, as well as policies and procedures. To search databases, keywords of sexual activity, sexual intercourse, sexual behavior, menstruation, menstrual bleeding, menstrual cycle, endometriosis and systematic reviews with their equivalent words in MeSH as well as their combination with each other were searched using Boolean operators (AND as well as OR). The PRISMA 2020 flowchart for systematic reviews was used to present the selection process for the studies.

### Study selection and data extraction

Titles and/or abstracts of studies obtained by the

search strategy and those obtained from extra sources were separated by two of our team members to find studies that potentially meet the aims of this study. The full text of these possibly appropriate articles was retrieved and evaluated independently for eligibility by another member of the research team. They separately reviewed the quality and acceptability of the articles, and any disputes were resolved by agreement with the third members of the team.

### Evaluation of methodological quality

To evaluate the quality of non randomized studies, Newcastle-Ottawa Quality Assessment Scale was used. Three classes of poor, moderate and good quality were identified. The cut-off points included: i. obtained score >75%: high methodological quality with 12 stars, ii. 50% < obtained score <75%: moderate methodological quality with 9-11 stars, and iii. obtained score ≤50%: low methodological quality with 0-8 stars. Each study was awarded a maximum of one star for each numbered item within the Selection and Exposure categories. Also, a maximum of two stars was given for Comparability. The study was categorized methodologically as high quality, if it achieved >75% of the score (29). The score of each item of the checklist was evaluated independently, in duplicate, by two researchers.

### Data collection

A validated data collection form was tabulated for data extracted from each study. This approach helped reviewers to analyze systematically. These extracted data for each study were composed of year of publication, study population, study design, participant number, outcome measure, and summary of results, conclusion and quality assessment score. Data were extracted by two authors (SM and MM), independently.

### Data analysis

The odds ratio (OR) (95% confidence interval [CI]) was used to express main effect size. Because of the high level of heterogeneity ( $I^2 > 75\%$ ) "random effect model" was used instead of "fixed effect model". For heterogeneity evaluation,  $I^2$  statistic was used. Review Manager (Rev Man) version 5.3 was used for the meta-analysis.

## Results

The selection process is accessible in the Figure 1. We found 1905 studies of associated databases. In the first step, 1405 studies were removed based on our criteria. In the second step, 416 studies that did not examine the relationship between the outcome variables, were omitted. And also, we miss 8 studies that did not analyze the association between sexual activity during menstruation and endometriosis. Finally, four studies were involved in the systematic review and meta-analysis.

**Table 1:** Characteristics of the included studies

Author (Ref.)	Year	Country	Study population	Study design	Cases	Controls	Outcomes measured	Results (n/N)	Conclusion	Quality score
Mollazadeh et al. (23)	2019	Iran	Women at reproductive age (20-50 years), who had undergone laparoscopy and open surgery with a histological diagnosis of endometriosis and population control	Case-control	185 women of reproductive age with confirmed endometriosis	370 women of reproductive age without endometriosis visiting the hospital for other issues	Number of women with history of coitus in case group and number of women without history of coitus in control group	Case: 30/185 Control: 28/370	There is an association between sexual activities during menstruation and endometriosis.	14
Meaddough et al. (26)	2002	USA	Women at reproductive age (Mean age: 35), with confirmed endometriosis and population control	Case-control	1,517 women of reproductive age from the Endometriosis Association in Milwaukee, Wisc.	495 women. Control group were recruited in two ways. 1- Association members who don't have endometriosis. 2- Members also consist of doctors and other individuals with an interest in endometriosis.	Number of women with history of coitus in case group and number of women without history of coitus in control group	Case: 1,154/1,517 Control: 369/495	Sexual activity during menstruation may confer protection against endometriosis.	12
Samir et al. (25)	2011	Qatar	Women at reproductive age (23-48) clinically symptomatic for endometriosis, or infertility patients with conformed laparoscopy or laparotomy diagnose of endometriosis	Case-control	51 women with a history of coital habitus during menstruation and subsequently were examined by ultrasound trans abdominal transvaginal or both, before laparoscopy or surgery.	27 women with no history of coital habitus during menstruation and subsequently were examined by ultrasound trans abdominal transvaginal or both, before laparoscopy or surgery.	Number of women with history of coitus in case group and number of women without history of coitus in control group	Case: 34/51 Control: 9/27	Coitus during menses could be a predisposing factor for endometriosis.	6
Filer and Wu (24)	1989	USA	Women at reproductive age in a private obstetrics-gynecology practice with conformed laparoscopy or laparotomy diagnose of endometriosis	Case-control	498 women with a history of coital habitus during menstruation	498 women with no history of coital habitus during menstruation	Number of women with history of coitus in case group and number of women without history of coitus in control group	Case: 87/498 Control: 54/498	The frequency of endometriosis was higher (P less than .05) in patients with coitus during menses.	7

Ref; Reference, n; Number of women with or without history of coitus in each group and N; Number of women in each group.

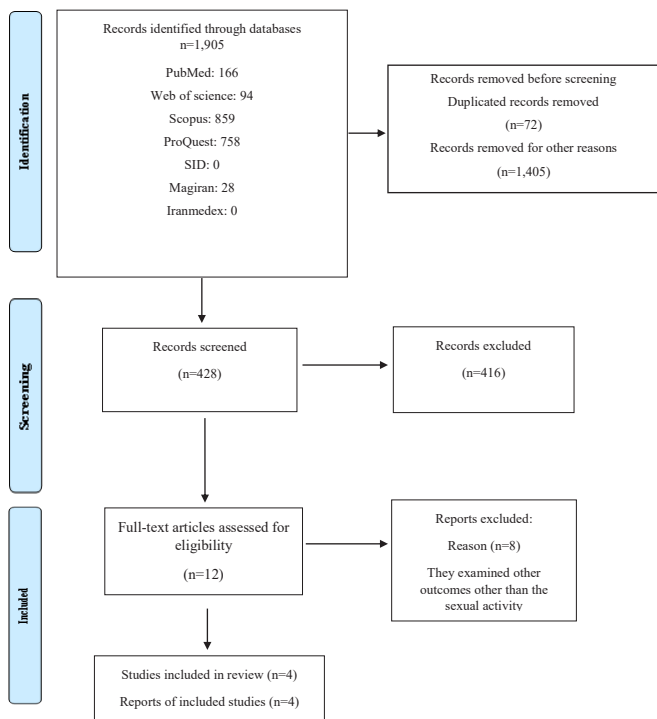


Fig.1: PRISMA Flow diagram of studies screening process.

The overall structure of the comprised studies were summarized in the Table 1. The included studies included two cross-sectional (24, 25) and two case-control (23, 26) studies, which were conducted and published between 1989 and 2019. In all studies, sexual activity during menstruation, as a risk factor for endometriosis, were analyzed.

Among these four studies, one was conducted in the Iran by Mollazadeh et al. (23), one in Qatar by Samir et al. (25) and two studies in the United States by Filer and Wu (24) and Meaddough et al. (26). The results of the first three studies showed that sexual activity during menstrual bleeding can increase the risk of endometriosis, while the last one, i.e. study by Meaddough et al. (26) showed that sexual activity may have a protective effect on endometriosis.

The results of the methodological quality evaluation by Newcastle-Ottawa Quality Assessment Scale showed that both studies by Mollazadeh et al. (23) and Meaddough et al. (26) were categorized in a high methodological quality with 14 and 12 stars, respectively [achieved score >75%]; whereas Samir et al (25) and Filer and Wu (24) studies were categorized in low methodological quality with 6 and 7 stars, respectively [achieved score ≤50%].

The results of meta-analysis on 3641 participants (2251 cases and 1390 controls) revealed approximately two times higher probability of having sexual activity during menstruation in the case group in comparison with the control group was (OR=1.80, 95% CI: 1.12 to 2.90, P=0.02). The heterogeneity was higher (I<sup>2</sup>=78%, Tau=0.17, Chi<sup>2</sup>=13.72, P=0.003, Fig.2).

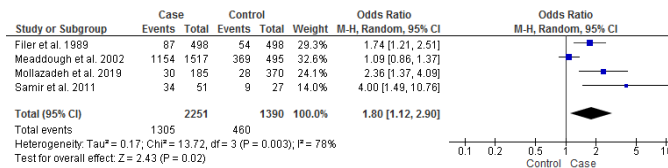


Fig.2: Association between sexual activity during menstruation and endometriosis.

## Discussion

Endometriosis is a problematical disease that disturbs the most important aspects of reproductive age women's life, such as fertility (19, 30, 31). Some studies showed that the sexual activity during menstruation increase the risk of endometriosis (23-25).

There are generally three theories about the pathogenesis of endometriosis, including: i. Celomic metaplasia, ii. residual embryonic Müllerian duct, iii. retrograde menstruation. Since retrograde menstruation is considered the main etiology of the endometriosis development, it is assumed that sexual activity during menstruation may possibly rise retrograde menstruation, the seed endometrial tissue in other places, and thus end to the risk of endometriosis. The existing systematic review and meta-analysis aimed to respond the question whether sexual activity through menstruation can be related to the occurrence of endometriosis. Up to now, four studies (23-26) have studied the relationship between sexual activity during menstruation and endometriosis.

The results of all three studies by Mollazadeh et al. (23), Samir et al. (25) and Filer and Wu (24) were consistent and showed that sexual activity during menstrual bleeding can increase the risk of endometriosis. They inferred that sexual activity during menstruation may rise the risk of retrograde menstrual bleeding, thereby, increase the probability of seeding endometrial tissue in places other than the endometrial cavity, while the studies showed that women who were less eager to have sexual activity during menstruation were more likely to develop endometriosis; So sexual activity may have a protective effect on the endometriosis. This issue is due to misinterpretation of the results, because sexual activity does not have a protective effect on the endometriosis. Women with endometriosis are reluctant to have sexual activity due to pain during intercourse (dyspareunia). They inferred that a probable clarification for these results, on the contrary, is the inadequacy of research tools or existence of confusing variables such as dyspareunia that were not involved in the questionnaire. Also, they inferred sexual activity may cause more effective menstrual discharge clearance of the vaginal vault, which in turn may facilitate cervical outflow, which Meaddough et al. (26) have mentioned well in the discussion section of their article.

Sexual activity during menstruation is a forbidden Islamic behavior that has been written in the Holy Qur'an

in Aya 222 of the Surat Al Baqarah: Avoid intercourse with menstruated wife until the end of their period is one of Islam religion rules (32). Relatively, ethical philosophies associated with sexual intercourse during menstrual bleeding are also introduced by the fuqaha and the Shari'a. All of them advise not to have sexual activity with women until their menstrual bleeding is over (29, 33).

In Christianity, similar to Islam, it is emphasized to avoid intercourse with women during menstrual bleeding. Judaism has wide laws (laws of niddah or family purity) that emphasize the avoidance of any sexual contact between couples during uterine bleeding, which is not due to a wound or uterine injury (28).

Avicenna in his book titled "The Canon of Medicine" has stated that it would be better if sexual intercourse takes place after a woman is cleansed of menstruation (34).

The strength of this systematic review was that selection of women with endometriosis was based on definitive histological analysis of endometriosis by laparoscopy in all included studies. This study had also some limitations; two included studies in the present review had low methodological quality. Also, the method for assessing the sample size in three of the included studies was not mentioned. Other limitation comes from more heterogeneous results across studies as well. For this reason, further studies with stronger designs are recommended.

## Conclusion

According to our results, sexual activity during menstruation can be a predisposing risk factor for endometriosis. Proper health education for women of reproductive age can promote their health and also, prevents endometriosis. The findings of this study can be used as a guide for medical staff in transmitting correct information to women of childbearing age. The midwife consultants, particularly, can benefit from such knowledge and in order to improve young girls and women's sexual health.

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## Authors' Contributions

S.M., R.L.R.; Have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data. Kh.M.N., M.M.; Have made substantial contributions to analysis of data. All authors have been involved in drafting the manuscript or revising it critically for important intellectual content. All authors read and approved the final manuscript.

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