Minimal and mild endometriosis negatively impact on pregnancy outcome

Luiz Fernando Pina Carvalho[1,2], Alexandra Below[1], Mauricio S. Abrão[2], Ashok Agarwal[1,3]

[1]Center for Reproductive Medicine, Obstetrics and Gynecology and Women's Health Institute, Cleveland Clinic, Cleveland, Ohio, USA
[2]Department of Obstetrics and Gynecology, Universidade de São Paulo (USP), São Paulo, SP, Brazil
[3]Glickman Urology and Kidney Institute, Cleveland Clinic, Cleveland Ohio, USA

Summary

Endometriosis, a highly prevalent gynecological disease, can lead to infertility in moderate to severe cases. Whether minimal stages are associated with infertility is still unclear. The purpose of this systematic review is to present studies regarding the association between pregnancy rates and the presence of early stages of endometriosis. Studies regarding infertility, minimal (stage I, American Society of Reproductive Medicine [ASRM]) and mild (stage II, ASRM) endometriosis were identified by searching on the MEDLINE database from 1985 to September 2011 using the following MESH terms: endometriosis; infertility; minimal; mild endometriosis; pregnancy rate. 1188 articles published between January of 1985 and November of 2011 were retrieved; based on their titles, 1038 citations were excluded. Finally, after inclusion and exclusion criteria, 16 articles were selected to be part of this systematic review. Several reasons have been discussed in the literature to explain the impact of minimal endometriosis on fertility outcome, such as: ovulatory dysfunction, impaired folliculogenesis, defective implantation, decrease embryo quality, abnormal immunological peritoneal environment, and luteal phase problems. Despite the controversy involving the topic, the largest randomized control trial, published by Marcoux et al. in 1997 found a statistically different pregnancy rate after resection of superficial endometrial lesions. Earlier stages of endometriosis play a critical role in infertility, and most likely negatively impact pregnancy outcomes. Further studies into stage I endometriosis, especially randomized controlled trials, still need to be conducted.

Keywords: Endometriosis; infertility; minimal endometriosis; stage I/II endometriosis; pregnancy outcome; systematic review.

Resumo

Endometriose mínima e leve e seu impacto negativo sobre a gravidez

O objetivo desta revisão sistemática é apresentar estudos sobre a associação entre as taxas de gravidez e a presença de fases iniciais de endometriose. Estudos relacionados com a infertilidade e estágios mínimos e leves (estágios I,II, American Society of Reproductive Medicine [ASRM]) foram identificados por busca na base de dados MEDLINE, de 1985 a setembro de 2011. Os seguintes termos foram usados como palavras-chave: endometriose, infertilidade, taxa de gravidez; estágio mínimo; estágio leve de endometriose. Entre janeiro de 1985 e novembro de 2011, 1188 artigos foram recuperados; com base no título, 1038 citações foram excluídas e, finalmente, depois de critérios de inclusão e exclusão, 18 artigos foram selecionados para fazer parte desta revisão sistemática. Várias razões têm sido discutidas na literatura na tentativa de explicar o impacto da endometriose mínima no resultado da fertilidade, tais como: disfunção ovulatória, foliculogênese alterada prejudicada, defeito na implantação, baixa qualidade embrionária, ambiente peritoneal inflamatório e hostil e problemas da fase lútea. Apesar de toda polêmica envolvendo o tópico, o maior ensaio clínico randomizado foi publicado por Marcoux *et al.* Os autores encontraram uma taxa de gravidez estatisticamente significante após a ressecção de lesões superficiais de endometriose. Estágios iniciais de endometriose desempenham um papel crítico relacionado à infertilidade e, provavelmente proporcionam um impacto negativo nas taxas de gravidez em pacientes com endometriose. Outros estudos envolvendo estágios iniciais de endometriose, especialmente ensaios clínicos randomizados, ainda precisam ser realizados.

Unitermos: Endometriose; infertilidade; endometriose mínima; endometriose leve; revisão sistemática; estágio I endometrioses; estágio II endometrioses; ASRM.

Study conducted at Cleveland Clinic, Ohio, USA

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Correspondence to:
Ashok Agarwal
Cleveland Clinic
9500 Euclid Avenue
Cleveland, OH 44195, USA
Phone: 216.444.9485
agarwaa@ccf.org

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Introduction

Endometriosis, a highly prevalent gynecological disease, can lead to infertility in moderate to severe cases[1]. Whether minimal stages are associated with infertility is still unclear**.** The relationship between infertility and endometriosis, though clinically recognized, is not clear[2]. In moderate to severe disease (stages III to IV, as outlined by the American Society of Reproductive Medicine [ASRM]), the association between infertility and endometriosis has been widely connected to severe pelvic adhesions. These adhesions can cause a variety of anatomical abnormalities such as cul-de-sac obliteration and large ovarian cysts, which can hinder ovum capture and transport[3-6]. The presence of these severely ectopic endometrial lesions is also known to decrease implantation rates[7], decrease oocyte retrieval rates, and decrease pregnancy rates when assisted reproductive technologies (ART) such as *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) are used[8].

However, in minimal (stage I) endometriosis, the relationship between infertility and the disease is not as evident because pelvic adhesions are not severe enough to create damaging anatomical effects. There are, however, possible mechanisms that could cause infertility in patients with mild disease, including ovulatory dysfunction, impaired folliculogenesis, defective implantation, eutopic endometrium abnormalities, abnormal immunological peritoneal environment, and luteal phase problems[8-13]. Despite these suggested mechanisms, the question remains whether endometriosis negatively impacts fertility when no anatomic alterations exist[14]. In order to improve the chances of infertile patients with endometriosis to become pregnant, physicians have essentially two options: surgery and ART. There is a consensus for the indication of surgery when the patients have severe pain; however, there is no consensus regarding whether surgery or ART should be performed as the first line of treatment on oligosymptomatic infertile patients with endometriosis. There is increased evidence that surgery for advanced stage of endometriosis improves IVF outcome. The effect of surgery on stage I/II is still debateable[15,16]. The purpose of this systematic review is to present the most up-to-date studies regarding the association between minimal to mild endometriosis and infertility. Specifically, studies that assess the association between pregnancy rates and the presence of stage I endometriosis in patients who had laparoscopic surgery or underwent various ARTs will be reviewed.

Methods

Relevant studies were identified by searches of the MEDLINE database from 1985 to September 2011. Electronic searches were conducted, using the following MESH terms: endometriosis; 69 infertility; minimal endometriosis; mild endometriosis; stage I and stage II ASRM. A manual search of references was performed for additional article retrieval. Review articles, editorials, and repeated manuscripts were excluded. Only manuscripts written in English were included. All included data were extracted independently by two different authors. The electronic search strategy of MEDLINE is available in the Appendix. The initial MEDLINE search using the search terms previously noted produced 1188 articles. Based on their titles, 1038 citations were excluded. Abstracts of the remaining studies (n = 150) were examined and, if relevant, were selected to be read in unabridged form. These studies were then reviewed using the final inclusion criteria, which included original articles published in English that measured pregnancy outcomes in endometriosis. Thirty-five articles were selected. Studies that did not include minimum to mild endometriosis were excluded. 16 articles were thus selected to be part of the review (Figure 1).

The following information was extracted from the 16 studies: (1) study design, (2) number of patients involved, (3) endometriosis stage, (4) control group, (5) ARTs employed, and (6) outcome/results with statistical significance (Table 1).

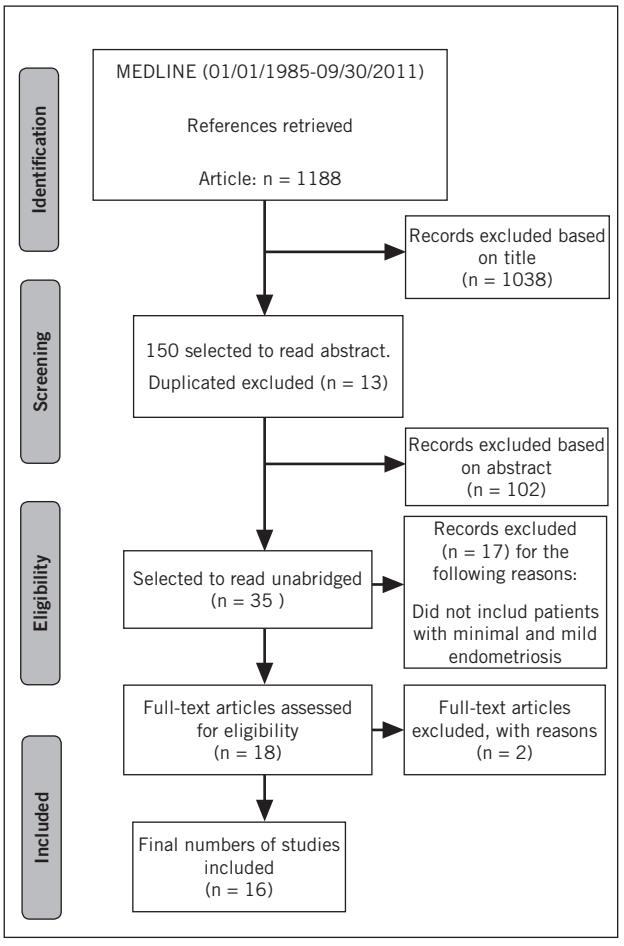

Figure 1 – Methods of systematic review.