



Review

Endometriosis and type 1 allergies/immediate type hypersensitivity: a systematic review



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ABSTRACT

Endometriosis is a chronic and debilitating disorder affecting up to 5–10% of women in reproductive age. Investigators have described deficiency in cellular immunity in women suffering from endometriosis, and in the recent years endometriosis has been linked to other diseases, allergic disease being one of them. The objective of this paper is to systematically review the existing literature on the possible association between endometriosis and allergic disease. This review is based on the recommendations by the preferred reporting of systematic reviews and meta-analysis (PRISMA) statement.

PubMed and Embase were searched for studies on women diagnosed with endometriosis and with manifestations of allergic disease who were compared to a reference group. Out of 316 articles screened, 6 were reviewed and 5 ultimately met the inclusion criteria. Four out of the five studies reported a positive correlation between endometriosis and allergic manifestations, including hay fever, sinus allergic rhinitis, and food intolerance/sensitivities (food allergy). Investigators reported an odds ratio (OR) as high as 4.28 (95% CI: 2.93–6.27) for a positive history of allergy among women suffering from endometriosis. Equivocal results were found on asthma prevalence in women with endometriosis. Due to the heterogeneity of the included studies, no meta-analyses could be performed.

The available literature clearly indicates that women with endometriosis are at an increased risk of allergic disorders compared to controls, but due to the lack of a concise definition of allergic disease and therefore diagnostic criteria, further studies are needed in order to draw firm conclusions on the association between endometriosis and allergic disease.

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Introduction

Endometriosis is defined by the presence of functional endometrial tissue outside the uterine cavity, usually located in the pelvis, but can also be present in other regions [1].

The prevalence of endometriosis is estimated to be 5–10% of women of reproductive age and as high as 30–50% in symptomatic women. Most women with endometriosis typically suffer from different pelvic pain symptoms, including dysmenorrhea, dyspareunia and pain during ovulation [1,2]. Furthermore, the prevalence of infertility among women suffering from endometriosis is as high as 30–50% [3]. Existing treatment for pain and infertility includes hormone therapy and surgical removal of implants/lesions [4]. Despite extensive treatment many women still suffer from frequent symptoms, in particular chronic pelvic pain. Endometriosis has an impact on education, work and social well being resulting in a lower quality of life for women affected by this enigmatic disease [5]. Additionally, the economic burden of endometriosis is substantial [6].

Multiple hypotheses have been proposed regarding the aetiology of endometriosis, with one of the most accepted being Sampson's theory of retrograde menstruation [7]. However, since retrograde menstruation is a common phenomenon in reproductive women, other mechanisms must be involved in the formation of endometriotic implants. Despite numerous research efforts the pathogenesis of endometriosis remains unknown.

Deficiency in cellular immunity in women suffering from endometriosis was first described in 1981 [8]. The investigators speculated if women with endometriosis "may have an incidence or a natural course of allergic, autoimmune or neoplastic diseases that are different from the general public" and in recent years several investigators have indeed reported that women with endometriosis seem to have an increased risk of developing allergic disorders [9–12]. Confirmation of a possible association could be a valuable step towards elucidating the pathophysiology of endometriosis.

Therefore, the purpose of this paper was to review the existing literature on the association between endometriosis and allergic disorders.

Hypersensitivity and allergic reactions

Allergic disease is a common cause of chronic illness in developed countries, and its prevalence seems to be rising [13]. In a Swedish study the rate of self reported food allergy in the age group 20–44 was 25% and symptoms were more common in women than in men (28% and 21% respectively $p < 0.1$) [14]. Another study conducted in Germany found the lifetime prevalence of medically diagnosed allergic disease to be 37.3% (95% confidence interval (CI): 33.2–41.7) among women in the age 18–29 years and for women between 30 and 39 years the prevalence was 42.2% (95% CI: 37.2–47.4) [15].

Although allergy is a term commonly used to describe all sorts of unexpected reactions in the skin and mucous membranes, type I allergy – immediate type hypersensitivity – is a distinct immunologic reaction, mediated by specific IgE antibodies bound

to the surface of mast cells and basophils [16]. See Supplemental material on the pathophysiology of type 1 allergies.

Typical symptoms and manifestations of type I allergic disease includes asthma, rhino-conjunctivitis, gastrointestinal symptoms and characteristic skin lesions (urticaria).

It is important to distinguish between different types of allergic reactions, as the immunological effector mechanisms are different. The type 1 allergy, immediate hypersensitivity, is an allergic reaction due to the production of IgE antibodies against otherwise harmless antigens. The type IV or delayed type hypersensitivity involves antigen specific T-cells, and clinically presents itself as contact dermatitis [17]. Eczema however can also be present without any allergy as seen in irritant/toxic contact dermatitis, atopic dermatitis and dyshidrotic eczema [17,18].

Materials and methods

The conduct and report of this review is based on the guidelines for the preferred reporting of systematic reviews and meta-analyses (PRISMA) [19], but was not preceded by a review protocol.

Search strategy

We performed a systematic literature search in PubMed and Embase for relevant studies published in the period 1980–January 2014. The search was made independently by two of the authors, HFB and UBK. For the database searches, the search terms "hypersensitivity" and "endometriosis" were used as Mesh/Emtree terms. To be certain that new, non-indexed studies were included, the search was expanded to include free text terms. Citations within the retrieved publications were examined for additional relevant articles.

Study selection criteria

The titles and abstracts were screened for the study design and measures of outcome and exposure. The included studies had to encompass a study group of women with a diagnosis of endometriosis and with manifestations of allergic disease, compared to a reference/control group. The studies had to be published as full-length articles in English. After these criteria were applied, five studies were found to be relevant for this review.

Quality assessment and data extraction

The Newcastle-Ottawa scale was used for assessing the quality of the included case-control studies. The studies were judged on the three perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of the exposure. The studies were scored independently by HFB and UBK and discussed where inconsistency occurred. Because of the heterogeneity of the included studies we did not deem a meta-analysis suitable and a principal summary measure cannot be found. The articles considered relevant were critically read in full and were evaluated. Data were extracted using a data extraction

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