Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 79 (2016) 577−582

www.jcma-online.com

Review Article

Women with endometriosis have higher comorbidities: Analysis of domestic data in Taiwan

Sen-Wen Teng [a,b], Huann-Cheng Horng [c,d], Chi-Hong Ho [c,d], Ming-Shyen Yen [c,d], Hsiang-Tai Chao [c,d], Peng-Hui Wang [c,d,e,*], The Taiwan Association of Gynecology Systematic Review Group [**]

[a] *Department of Obstetrics and Gynecology, Cardinal Tien Hospital-Hsintien, New Taipei City, Taiwan, ROC*
[b] *Department of Obstetrics and Gynecology, Fu Jen Catholic University, New Taipei City, Taiwan, ROC*
[c] *Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[d] *Department of Obstetrics and Gynecology, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*
[e] *Department of Medical Research, China Medical University Hospital, Taichung, Taiwan, ROC*

Received October 12, 2015; accepted April 13, 2016

Abstract

Endometriosis, defined by the presence of viable extrauterine endometrial glands and stroma, can grow or bleed cyclically, and possesses characteristics including a destructive, invasive, and metastatic nature. Since endometriosis may result in pelvic inflammation, adhesion, chronic pain, and infertility, and can progress to biologically malignant tumors, it is a long-term major health issue in women of reproductive age. In this review, we analyze the Taiwan domestic research addressing associations between endometriosis and other diseases. Concerning malignant tumors, we identified four studies on the links between endometriosis and ovarian cancer, one on breast cancer, two on endometrial cancer, one on colorectal cancer, and one on other malignancies, as well as one on associations between endometriosis and irritable bowel syndrome, one on links with migraine headache, three on links with pelvic inflammatory diseases, four on links with infertility, four on links with obesity, four on links with chronic liver disease, four on links with rheumatoid arthritis, four on links with chronic renal disease, five on links with diabetes mellitus, and five on links with cardiovascular diseases (hypertension, hyperlipidemia, etc.). The data available to date support that women with endometriosis might be at risk of some chronic illnesses and certain malignancies, although we consider the evidence for some comorbidities to be of low quality, for example, the association between colon cancer and adenomyosis/endometriosis. We still believe that the risk of comorbidity might be higher in women with endometriosis than that we supposed before. More research is needed to determine whether women with endometriosis are really at risk of these comorbidities.

Keywords: comorbidity; endometriosis; Taiwan

1. Introduction

Endometriosis, one of the most common gynecologic disorders, is found in 1−30% of women during their reproductive years, based on the different diagnostic criteria, and sometimes occurs in postmenopausal women. It is found in 70−90% of women with pelvic pain symptoms.[1−3] Endometriosis remains an enigmatic disease and cause of pain, and can subsequently result in pelvic inflammation, adhesion, chronic pain, and

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail addresses: phwang@vghtpe.gov.tw, phwang@ym.edu.tw, pongpongwang@gmail.com (P.-H. Wang).
** The members of the Taiwan Association of Gynecology Systematic Review Group are listed in Appendix 1.

http://dx.doi.org/10.1016/j.jcma.2016.04.006

infertility, and occasionally in malignant transformation.[4,5] Since endometriosis-associated morbidity shows a significant negative impact on women's quality of life, it contributes to a long-term major health issue. This study report addresses the associations between endometriosis and other diseases from the domestic source in Taiwan. The majority of the data are obtained from a large-scale population-based study—the National Health Insurance Research Database (NHIRD).[6,7]

2. Epidemiology

Epidemiologic studies may be helpful in defining populations at a high risk of endometriosis[1,3−5]; however, it is not easy to estimate the real incidence or prevalence of endometriosis precisely even when the gold-standard method, laparoscopy, is used. Variations may be influenced by the wide range of visual appearance of endometriosis and pathological confirmation, resulting in an unknown true prevalence or the real incidence of endometriosis. Hopton and Redwine[8] noted that the visual appearance of endometriosis is important because therapy begins with a surgeon identifying the disease, and any inaccurate identification of endometriosis can introduce selection bias and confound all conclusions, leading to incorrect concepts of epidemiology, natural history, disease origin, and treatment. In 1995, Chu and colleagues'[9] pioneered study of the prevalence of endometriosis in Taiwan showed a wide variation (5−42%) on the basis of different indications for 752 consecutive laparoscopic procedures. The prevalence of endometriosis was 42%, 33%, 25%, and 12%, respectively, in women indicated for pelvic adhesion, infertility, myoma, and sterilization; the researchers concluded that the overall prevalence of endometriosis in asymptomatic patients was 24.7%. This study was one of the earliest to investigate the prevalence of endometriosis in Taiwan. However, this study might overestimate or underestimate the prevalence of endometriosis in Taiwan. Since surgery is always applied in a certain type of population, for example, women with needs and indications, surgery itself might be one of the most significant confounding factors, contributing to the high possibility of selection bias. In addition, the "illusory tale of occult microscopic endometriosis" might underestimate the prevalence of endometriosis.[8] Endometriosis is sometimes truly invisible to the surgeon because it is too small to see.[8] In previous studies from Taiwan,[1,3−5] the prevalence of endometriosis also varied markedly. With different criteria applied for enrollment of patients with endometriosis, the prevalence might be different. A recent report by Lee et al[3] might be one of the best representatives. Their results showed that the prevalence of endometriosis during reproductive years could be up to 30.8% and as low as 1.5%.[3] The dramatic difference in the prevalence could be well explained by the different criteria applied in the study. Yang et al[1] showed that the estimated prevalence of women with endometriosis was 8.9% based on the NHIRD of Taiwan. However, only two-fifths of these women with a clinical diagnosis of endometriosis had a surgicopathological confirmation of their endometriosis, contributing to 3.7% of the prevalence rate,[3] which was significantly lower than the 5−10% rate found in literature reviews.[10]

3. Comorbidity of endometriosis

Previous research suggests that a comorbidity relationship exists between endometriosis and many functional and/or pathological diseases,[1,11,12] although the results of some studies were not consistent. For example, endometriosis was not associated with diabetes mellitus in one cross-sectional study,[13] and reports showed that women with endometriosis might have a lower body mass index and be less frequently obese[14,15]; however, domestic nationwide population-based studies showed that women with endometriosis seemed to have a tendency of being obese and a higher rate of diabetes mellitus.[4,5,11,12] One report showed 7.5% of women with diabetes mellitus in the endometriosis group compared with 5.8% in the nonendometriosis (control) group.[4] Another report found diabetes mellitus in 16% of women with endometriosis compared with that in 13% of women without endometriosis.[12] Besides a higher rate of diabetes mellitus in women with endometriosis, domestic data showed that Taiwanese women with endometriosis seemed to have a higher tendency to be obese.[11,12] This finding was different from those of previous reports from Western countries[14,15]—a discrepancy that needs further investigation. Of course, different criteria might have resulted in the different prevalence estimations, suggesting that sampling differences might have contributed to this finding.

A domestic study also found that a higher proportion of women with endometriosis had pelvic inflammatory disease (76.0% vs. 38.4%, endometriosis vs. controls, $p < 0.0001$), infertility (10.2% vs. 2.0%, $p < 0.0001$), cardiovascular diseases (4.9% vs. 3.5%, $p < 0.0001$), chronic liver disease (2.2% vs. 1.5%, $p = 0.0002$), and rheumatic disease (4.0% vs. 2.4%, $p < 0.0001$).[4] Similar findings were also reported from another domestic population-based study.[12] Wu et al[12] showed that women with endometriosis frequently had hypertension (24.0% vs. 20.6%, $p < 0.001$) and hyperlipidemia (28.7% vs. 23.0%, $p < 0.001$). Both hypertension and hyperlipidemia might be considered among the important components of cardiovascular diseases, suggesting that women with endometriosis are frequently associated with metabolic and cardiovascular problems. By contrast, a recent domestic study showed that women with endometriosis had a lower rate of hypertension than women without endometriosis. Although this study did not support a higher incidence of hypertension in women with endometriosis, the finding could be discarded, mainly because Yu et al's[11] study showed an unusually higher proportion of hypertension in their study population. More than one-half of their studied patients had hypertension status; this occurred in both cohort groups (50.7% of women with endometriosis and 55.7% of women without endometriosis, $p < 0.001$), suggesting that the study population might not really be representative of the general population. In addition, Yu et al[11] also showed an unusually higher proportion of study population with hyperlipidemia (53.9% and 44.9% in women with and without endometriosis, respectively; $p < 0.001$) and