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Prevalence and confounders of chronic endometritis in premenopausal women with abnormal bleeding or reproductive failure

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KEY MESSAGE

The prevalence of chronic endometritis was increased in women with recurrent implantation failure, abnormal uterine bleeding and endometrial hyperplasia compared with those without the respective conditions, and also significantly higher in the proliferative stage of menstrual cycle compared with the luteal phase.

A B S T R A C T

In this retrospective cohort study, a consecutive series of 1551 premenopausal women underwent hysteroscopy and endometrial biopsy. Chronic endometritis was diagnosed when plasma cell in endometrial tissue was detected by immunohistochemistry using CD138 epitope. The overall prevalence of chronic endometritis in the population studied was 24.4% The prevalence was significantly increased in the following conditions: recurrent implantation failure (40.8%; $P < 0.001$), abnormal uterine bleeding (40.7 %; $P < 0.001$), endometrial hyperplasia (50.0%, $P < 0.05$) and submucosal fibroid (59.1%; $P < 0.001$) than those without the respective conditions. The prevalence in specimens obtained from the proliferative phase (26.0%) was significantly higher ($P < 0.05$) than those from the luteal phase (17.5%). Logistic regression analysis showed three significant factors affecting the prevalence, in descending order of importance: clinical presentation, endometrial hyperplasia and stage of the cycle from which the specimen was obtained. The confounding variables identified in this study may account for the wide range of published prevalence of the condition, and should be considered in the analysis of prevalence data relating to chronic endometritis.

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Introduction

Chronic endometritis is a persistent inflammation of uterine endometrium. Histologically, the diagnosis of chronic endometritis is based on the presence of plasma cells in the endometrial stroma. The identification of plasma cell by the use of haematoxylin-eosin staining in wax-embedded endometrial specimen has been used for some time as the gold standard for the diagnosis of chronic endometritis (Crum et al., 1983; Greenwood and Moran, 1981). One challenge of haematoxylin-eosin staining is the identification of rare plasma cells, as these cells can appear morphologically similar to other stromal cells and leukocytes (Kannar et al., 2012). Recent studies have shown that the use of immunohistochemistry for CD138, a cell surface proteoglycan that is expressed on plasma cells, improves the diagnostic accuracy (Kitaya and Yasuo, 2013).

The prevalence of chronic endometritis in different populations, including women with abnormal uterine bleeding (AUB), recurrent implantation failure (RIF), recurrent pregnancy loss (RPL), infertility and intrauterine adhesion (IUA), has been examined by various investigators (**Table 1**). Few investigators, however, have simultaneously examined the prevalence in the different populations. It is difficult to compare the prevalence data from these various studies because the criteria used for the diagnosis of chronic endometritis is often different (**Table 1**). In addition, it is also possible that the prevalence may be affected by a number of confounding clinical and pathological conditions. For example, it has been reported that the prevalence of chronic endometritis may be affected by the stage of the cycle from which the specimen was obtained (Adegboyega et al., 2010). It is also unclear if certain uterine pathologies such as endometrial polyp, fibroid, endometrial hyperplasia or congenital uterine anomaly affect the prevalence of chronic endometritis.

The aim of the present study was to examine the prevalence of chronic endometritis in a consecutive series of endometrial biopsies obtained from premenopausal women who presented with abnormal uterine bleeding or reproductive failure, and to identify confounding variables that may affect the prevalence of chronic endometritis.

Table 1 – Reported prevalence of chronic endometritis in various populations studied and the criteria used for diagnosis.

Authors	Prevalence of chronic endometritis, n (%)	Diagnostic criteria used
Recurrent pregnancy loss		
Zolghadri et al., 2011	61/142 (43.0)	H&E > one plasma cell/HPF
Cicinelli et al., 2014	190/360 (52.8)	H&E > one plasma cell/HPF
McQueen et al., 2014	35/395 (8.9)	H&E > one plasma cell in whole section
McQueen et al., 2015	60/107 (56.1)	>one CD138⁺ cells/HPF
Bouet et al., 2016	14/51 (27.5)	≥five CD138⁺ cells/10 HPF
Recurrent implantation failure		
Johnston-MacAnanny et al., 2010	10/33 (30.3)	>one CD138⁺ cells/HPF
Cicinelli et al., 2015	61/106 (57.5)	H&E > one plasma cell/HPF
Bouet et al., 2016	6/43 (14.0)	≥f ive CD138+ cells/10 HPF
Abnormal uterine bleeding		
Bayer-Garner et al., 2004	20/47 (42.6)	>one CD138⁺ cells in whole section
Kannar et al., 2012	26/50 (52.0)	>one CD138⁺ cells/10 HPF
Infertility		
Kasius et al., 2011	17/606 (2.8)	>one CD138+ cells in whole section
Chen et al., 2016	9/37 (24.3)	>five CD138⁺ cells in whole section
Intrauterine adhesion		
Chen et al., 2016	29/82 (35.4)	H&E > one plasma cell in whole section

H&E, hematoxylin and eosinl; HPF, high power field.

Materials and methods

Participants

A total of 1551 premenopausal women referred to the Hysteroscopy Centre of Fu Xing Hospital, Capital Medical University, Beijing, for investigation of abnormal uterine bleeding or reproductive failure were included. All women underwent hysteroscopy and endometrial biopsy for histological analysis. The study was carried out between September 2014 and November 2016. The Hysteroscopic Centre of Fu Xing Hospital is a national training centre for hysteroscopy, in which about 10,000 cases of hysteroscopy are carried out annually among six consultant teams. The present study was recruited from patients attending one of the consultant teams.

The exclusion criteria included the following: menstruating at the time of examination; suspected reproductive tract infection; presence of intrauterine contraceptive device; history of endometrial carcinoma; pregnancy or pregnancy-related complications, i.e. retained product of conception; and hysteroscopic surgery within the last 3 months. The study was approved by the hospital Institutional Review Board on 1 August 2014 (reference number 2014 FXHEC-KY056).

Definitions

Recurrent pregnancy loss was defined as two or more clinical pregnancy losses (miscarriages) before 20 weeks' gestation (American Society for Reproductive Medicine, 2008). Recurrent implantation failure was defined as the failure to achieve a clinical pregnancy after transfer of at least four good-quality embryos in three or more transfer cycles in women younger than 40 years (Coughlan et al., 2014).

Hysteroscopy and endometrial biopsy

Hysteroscopy and endometrial biopsy were carried out as an outpatient procedure without anaesthesia. Hysteroscopy was carried out using a 3-mm 30° rigid hysteroscope (Olympus, Germany). Normal saline solution was used to distend the uterine cavity at 100 mmHg pressure. On completion of hysteroscopy, an endometrial biopsy was obtained with the use of a curette.

Histological analysis and immunohistochemistry

Endometrial samples were fixed in neutral formalin and later embedded in paraffin for histological analysis and immunohistochemistry.

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