

## High Prevalence of Chronic Endometritis in Recurrent Pregnancy Loss and in Repeated Implantation Failure.

慢性子宮內膜炎於反覆著床失敗或重複流產病人中具有高盛行率

溫仁育\* 蔡永杰 鍾明廷 林毅倫 林亮吟 陳嫻君 黃宣綺 林怡君 賴怡君  
奇美醫院婦產部生殖醫學科

Jen-Yu Wen\*, Yung-Chieh Tsai, Ming-Ting Chung, Billy Lin, Liang-Yin Lin, Irene Chen, Hsuan-Chi Huang, Yi-Chun Lin, I-Chun Lai,

Center for Reproductive Medicine, Depart of Obs Gyn, Chi-Mei Medical Center

### **Study Question:**

Chronic endometritis (CE) has been reported to have a higher prevalence rate in patients with recurrent pregnancy loss (RPL), repeated implantation failure (RIF), and unexplained infertility. (Farooki., 1967; Kimura et al., 2019) However, wide range of prevalence was reported owing to different diagnostic method. And still, there was study questioned the higher rate of CE in patient with infertility. (Kasius et al., 2012) This study was conducted to assess the prevalence of CE in patients with infertility, RPL, and/or RIF in our center.

### **Study Design, Size, and Duration:**

This is a retrospective study included females underwent endometrial biopsy for chronic endometritis diagnosis from Jan 2019 to Jun 2020 in our hospital. CE was diagnosed based on conventional histology and immunohistochemistry with anti-syndecan-1 antibodies to identify CD138 positive plasma cells of endometrial tissue. Totally 89 females were included, which consisted of 32 patients with RPL, 37 infertile patients with history of RIF, and 20 infertile females without RIF. Here, repeated implantation failure (RIF) was defined as no clinical pregnancy after transfer of at least 2 blastocysts, or no clinical pregnancy after transfer at least 3 good quality cleavage stage embryos, i.e. 4 cells on day 2 or 8 cells on day 3 with fragmentation <50%. Recurrent pregnancy loss (RPL) was defined as at least twice abortion before 20<sup>th</sup> gestational weeks. Prevalence of CE was calculated. Antibiotic treatment was given for patient diagnosed with CE. Pregnancy rate and ongoing pregnancy rate within 1 year after complete antibiotic treatment till the presented date was calculated and compared between positive CE and negative CE patients. An ongoing pregnancy was defined as each pregnancy showing a positive heartbeat at ultrasound after 12 weeks of gestation. Two-sample t-test, Mann-Whitney U tests, Chi-square tests, and Fisher's exact tests were used for statistical analyses. The P <

0.05 was considered statistically significant.

### **Main Results:**

#### **(1) Prevalence of chronic endometritis (Table 1)**

The overall prevalence of chronic endometritis diagnosis was 63.6% (56/88). In the 36 patient who had history of repeated implantation failure, the prevalence of CE was 52.8%(19/36). In the 32 patients who had history of recurrent pregnancy loss, the prevalence of CE was 78.1% (25/32). Even in the infertility patients who did not fulfill the criteria of RIF, the percentage of CE diagnosis was high (60%, 12/20).

#### **(2) Pregnancy rate and Ongoing pregnancy rate**

For infertile patients with RIF, the pregnancy rate was 29% (5/17) in patients with negative CD-138 immunostaining and 26.3% (5/19) in patient with positive CD-138 immunostaining after antibiotic treatment.(Table 2) For patients with RPL, the ongoing pregnancy rate was 28.6% (2/7) in patients with negative CD-138 immunostaining and 16% (4/25) in patient with positive CD-138 immunostaining after antibiotic treatment.(Table 3) None of them reached significant difference.

### **Conclusions:**

High prevalence of chronic endometritis in infertile women was noted in this study, even higher in patient with history of RPL and RIF. Though the positive effect to subsequent pregnancy outcome was not evident in this study. The elimination of the source of infection with antibiotic treatment can theoretically restore normal endometrial tissue and increase the pregnancy rate and live birth rate. Further well-designed prospective study should be conducted to investigate the possible effect of CE treatment on reproductive outcome.

Key Word: chronic endometritis (CE), recurrent pregnancy loss, recurrent miscarriage, repeated implantation failure, in vitro fertilization (IVF), assisted reproductive technology (ART), CD-138, immunostaining, Syndecan-1, treatment, pregnancy, live birth.

Table 1. Prevalence of chronic endometritis in recurrent pregnancy loss and in repeated implantation failure patients.

	RIF	RPL	Infertility	Total
<b>N</b>	36	32	20	88
<b>CE+ (Number)</b>	19	25	12	56
<b>CE+ (%)</b>	52.8%	78.1%	60.0%	63.6%

Table 2. Pregnancy rate and Ongoing pregnancy rate after antibiotic treatment in RIF patients

	CE+	CE-	P value
<b>No. of cases</b>	19	17	
<b>Age (y/o)</b>	38.0±4.3	37.8±5.1	0.865
<b>BMI (kg/m<sup>2</sup>)</b>	23.5±4.2	24.3±5.2	0.615
<b>Type of infertility</b>			0.194
<b>Primary</b>	68.4%(13/19)	47.1%(8/17)	
<b>Secondary</b>	31.6%(6/19)	52.9%(9/17)	
<b>Pregnancy rate</b>	26.3%(5/19)	29.4%(5/17)	0.836

mean±SD, %(n)

Table 3. Pregnancy rate and Ongoing pregnancy rate after antibiotic treatment in RPL patients

	CE+	CE-	P value
<b>No. of cases</b>	25	7	
<b>Age (y/o)</b>	34.8±5.1	37.5±4.0	0.327
<b>BMI (kg/m<sup>2</sup>)</b>	22.1±3.2	24.1±4.7	0.352
<b>Ongoing pregnancy rate</b>	16.0%(4/25)	28.6%(2/7)	0.590

mean±SD, %(n)