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Association between monocyte percentage and chronic endometritis among infertile patients: a retrospective study

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The diagnosis rate of chronic endometritis (CE), closely associated with infertility, recurrent pregnancy loss, and recurrent implantation failure, remains low in clinical practice. The monocyte percentage (MP) has been identified as a biomarker predicting prognosis in various severe diseases. Although monocytes have been linked to clinical endometritis in animals, their associations with CE in infertile patients remains unclear. This cross-sectional study included patients pathologically diagnosed with CE at a single center in 2021. Demographic data, history of abortion, causes of infertility, Ureaplasma urealyticum infection history, laboratory findings, and histological information were recorded. The correlation between MP and CE was investigated using logistic regression analysis, and subgroup analyses were conducted based on age, gravidity, parity, and follicular phase. The cohort consisted of 631 individuals, including 494 patients with CE, corresponding to a CE prevalence of 78%. Univariate logistic regression analysis revealed an inverse correlation between MP and CE risk (odds ratio [OR] = 0.85; 95% confidence interval [CL], 0.76–0.96; $P < 0.01$). Multivariate regression after adjusting for all covariates yielded an OR of 0.82 (95% CI 0.71–0.95). Furthermore, the stratified and subgroup analyses yielded consistent results. Sensitivity analyses excluding participants with pathological endometrial changes (OR = 0.83; 95% CI 0.71–0.96), those in the non-follicular phase (OR = 0.78; 95% CI 0.66–0.92), and those with both endometrial abnormality and non-follicular phase status (OR = 0.82; 95% CI 0.7–0.95) further confirmed the correlation between MP and CE risk. MP was significantly associated with CE in infertile participants in models adjusted for all covariates, suggesting that MP may be a valuable parameter for early CE prediction.

Keywords Chronic endometritis, Monocytes percentage, Infertility

Chronic endometritis (CE), a subtle pathological condition characterized by abnormal infiltration of plasma cells into the endometrial stroma, primarily manifests as chronic local inflammation. Although patients with CE may exhibit symptoms such as abnormal vaginal discharge, dysfunctional uterine bleeding, dyspareunia, or pelvic pain[1], the disease is often underdiagnosed because it is asymptomatic or only mildly symptomatic. However, increasing evidence suggests that CE is closely associated with adverse perinatal and neonatal outcomes, as well as infertility.

It has been reported that approximately 2.8–56.8% of infertile patients[2], 14.0–67.5% of recurrent implantation failure (RIF) patients[3], and 9.3–67.6% of recurrent pregnancy loss (RPL) patients[4] are affected by CE. However, the need for an endometrial biopsy and histopathological evaluation limits the identification of patients in clinical practice. The detection of plasma cells primarily relies on laboratory methods such as hematoxylin–eosin (H&E) staining and immunohistochemical (IHC) testing for the plasma cell-specific surface antigen CD138. Positive CD138 expression provides higher sensitivity for diagnosing CE, thereby reducing the risk of misdiagnosis or missed diagnosis and minimizing observer-related variability among pathologists[5,6].

Under physiological conditions, the human endometrium is infiltrated by various immune cells types, including macrophages, T cells, natural killer (NK) cells, and neutrophils. However, in patients with CE, plasma cells differentiated from B lymphocytes can infiltrate the endometrium. Matteo et al.[7] reported reduced endometrial T-cell infiltration in infertile patients with CE compared to those with unexplained infertility. Wang et al.[8] found that, in patients with CE, an increased proportion of endometrial Th17 cells and decreased

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expression of TGF-β and IL-10 disrupted the Th17/Treg balance. In addition, decreased expression of the chemokines CCL4 and MIP-1β, which recruit macrophages and NK cells, has been observed[9].

Monocytes are crucial components of the innate immune system. Therefore, the monocyte percentage (MP) has been widely used as a key marker for predicting the prognosis of various pathological conditions associated with immune dysfunction, including malignancies[10], chemotherapy response[11], deep vein thrombosis in patients with ovarian cancer[12], aseptic Lymphocytic-Dominated Vasculitis[13], and chronic obstructive pulmonary disease[14]. Monocytes have also been linked to CE in animal models such as dromedary camels[15] and cows[16]. However, to our knowledge, whether MP is associated with CE in humans remains elusive until now. Therefore, we conducted this cross-sectional study to investigate the correlation between MP and CE risk in a cohort of infertile patients.

Methods

The study included 746 infertile individuals who underwent hysteroscopic endometrial tissue biopsy and CD138 immunohistochemistry(IHC) analysis at the Department of Gynecology, Guangdong Women and Children Hospital, in 2021 for infertility evaluation. The study protocol was approved by the Ethics Committee of Guangdong Women and Children Hospital (approval number: 202401137) and was conducted in accordance with the Declaration of Helsinki.Since this was an anonymous retrospective analysis, the Ethics Committee of Guangdong Women and Children Hospital approved the waiver of informed consent. After excluding patients from the inpatient and gynecology outpatient departments and those with missing monocyte percentage data, 631 participants were finally included, comprising 137 CD138-negative and 494 CD138-positive cases. Figure 1 illustrates the overall participant enrollment process.

Clinical characteristics

General clinical information was collected, including age, gravidity, parity, mode of delivery (vaginal or cesarean section), history of abortion, ectopic pregnancy, causes of infertility, Ureaplasma urealyticum (UU) infection history, laboratory test results, and histological findings related to the endometrial phase, polyps, and hyperplasia.

MP was calculated as the ratio of monocytes to total white blood cells, derived from participants' laboratory test records. Peripheral MP values were obtained from routine complete blood counts with five-part differential analyses (absolute and percentage counts of lymphocytes, monocytes, eosinophils, basophils, and neutrophils) performed at diagnosis using a fully automated hematology analyzer (Mindray, China). Peripheral MP was expressed as a percentage, calculated by dividing the absolute monocyte count by the total leukocyte count and multiplying by 100.

All patients underwent hysteroscopy performed by an experienced surgeon. During the hysteroscopic endometrial biopsy, tissue specimens were collected using biopsy forceps and examined independently by two specialists to evaluate pathological changes in the endometrium. The specimens were immediately fixed in 10% neutral formaldehyde, embedded in paraffin wax, and sectioned into 4-μm-thick slices. These sections were used for H&E staining and IHC analysis. For IHC assays, a commercial kit (CELNOVTE, China) was used. The detection of plasma cells within the endometrial stroma, assessed using CD138 IHC staining, served as the histological diagnostic criterion. After initial low-magnification screening, the number of plasma cells per 400 × high-power field (HPF) (CD138/HPF) was quantified to determine the maximum plasma cell count. In this study, the diagnosis of CE was established by considering both pathological and histological findings from CD138 IHC staining. Specifically, the concurrent presence of plasma cells on H&E staining and ≥ 1 CD138-positive cell per 10 high-power fields in IHC assay was deemed indicative of a positive CE case[17–19].

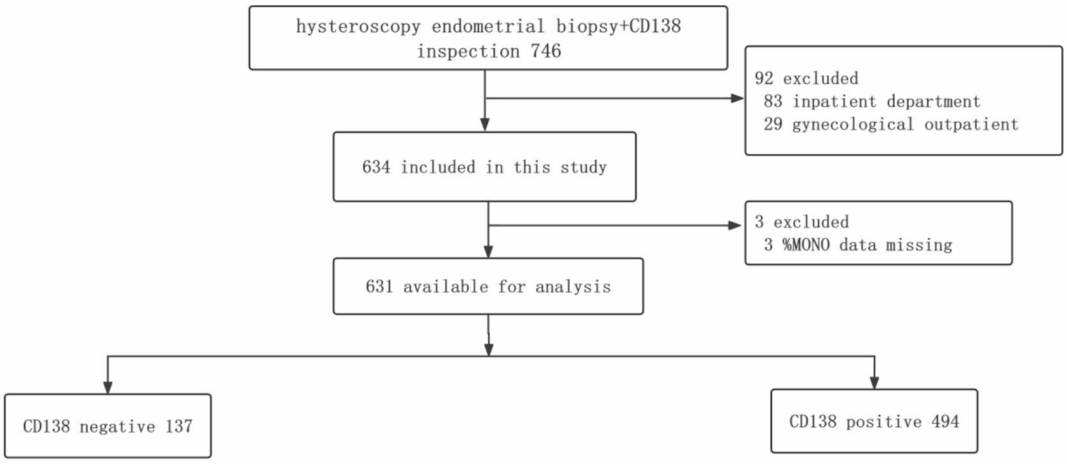

Fig. 1. Flow diagram of the screening and enrollment of study participants.

Statistical analysis

All analyses were performed using R version 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org) and Free Statistics software version 1.7. A two-sided P value < 0.05 was considered statistically significant. Independent t tests and $\chi 2$ tests were conducted to analyze differences in quantitative and qualitative variables, respectively. Data imputation was not performed because of the low proportion of missing data.

The correlation between MP and the incidence of CE was examined using six logistic regression models. Model 1 was unadjusted. Model 2 was adjusted for age, gravidity, parity. Model 3 was adjusted for the variables in Model 2 plus endometrial phase (follicular, middle, and luteal). Model 4 was adjusted for the variables in Model 3 plus histological findings (polyp, hyperplastic polyp, and hyperplasia). Model 5 was adjusted for the variables in Model 4 plus reproductive and clinical factors, including induction of labor, medical abortion, artificial abortion, curettage, spontaneous abortion, inevitable abortion, habitual abortion, ectopic pregnancy, primary infertility, chromosomal abnormalities, ovarian factors, polycystic ovary syndrome (PCOS), fallopian tube factors, endometriosis, pelvic inflammatory disease, male factors, unfavorable pregnancy history, and UU infection history. Model 6 was adjusted for the variables in Model 5 plus neutrophil (NEUT), lymphocyte (LYMPH), and platelet (PLT) counts. The participants were also stratified based on age, gravidity, parity, and follicular phase, and the correlation between MP and CE incidence was further investigated within these subgroups. In addition, the following sensitivity analyses were conducted to assess the robustness of the findings: (1) excluding participants with endometrial abnormalities; (2) excluding participants in the non-follicular phase; (3) excluding participants with both endometrial abnormalities and non-follicular phase.

Results

Characteristics of the participants

Based on the inclusion and exclusion criteria shown in Fig. 1, this study ultimately included 631 participants, whose demographic characteristics are summarized in Table 1. The cohort comprised infertile patients with a mean age of 32.5 years, and the age range peaked age between 22 and 47 years. CE was diagnosed based on the pathological and histological findings in 494 participants, corresponding to a prevalence of 78%. According to CD138 status, the cohort was divided CD138-positive and CD138-negative groups, with mean ages of 32.4 ± 5.0 and 32.6 ± 4.6 years, respectively. Significant differences in endometrial phase, endometrial hyperplastic polyp, and PLT levels (P < 0.05 for all parameters) were observed between the CD138-negative and CD138-positive groups. A higher proportion of the histological endometrial phase was noted in the CD138-positive group (P < 0.05). CD138-positive individuals exhibited a higher frequency of histological hyperplastic polyps (62 vs. 5, P = 0.003) and higher PLT levels (P = 0.005) compared with CD138-negative individuals.

CE-associated factors

Factors correlated with CE incidence were initially examined in the participant cohort using univariate ordinal regression analysis. As shown in Table 2, the endometrial phase, endometrial hyperplastic polyp, and PLT levels were identified as factors positively associated with CE positivity (P < 0.05 for all parameters).

Correlation of MP with CE incidence

As shown in Table 3, a significant association was observed between MP and the CE incidence. Specifically, the risk of histologically confirmed CE increased as MP levels decreased, with a non-adjusted odds ratio (OR) of 0.85 (95% CI 0.76–0.96). After adjusting for all covariates, the OR was 0.82 (95% CI 0.7–0.95). The statistical results remained robust across all models (Table 3).

Subgroup analyses

The infertile participants were then divided into subgroups stratified by age, gravidity, parity, and endometrial follicular phase (Fig. 2). The effect size of MP on the presence of CE remained stable across subgroups. Among CE-positive participants, the interactions between MP and age (P = 0.869), parity (P = 0.114), and endometrial follicular phase (P = 0.567) were not significant.

Sensitivity analyses

The sensitivity analysis findings are summarized in Table 4. When participants with endometrial abnormalities (n = 540) were excluded, MP remained associated with CE (OR = 0.83; 95% CI 0.7–0.96). When non-follicular phase participants (n = 547) were excluded, the OR was 0.78 (95% CI 0.66–0.92). In addition, after excluding participants with both endometrial abnormalities and non-follicular phase (n = 468), the association between MP and CE persisted (OR = 0.82; 95% CI 0.7–0.95).

Discussion

There is currently no early or simple marker of CE, particularly in infertile patients. In this cross-sectional study, the MP was found to be associated with CE in infertile patients for the first time. Specifically, MP levels were inversely correlated with CE incidence in the study population. This association remained significant in the adjusted models. These findings highlight the potential value of MP as a predictive marker for CE development.

Monocytes are crucial components of innate immunity and circulate in the bloodstream. Upon activation by various inflammatory stimuli, they are recruited to sites of inflammation, where they differentiate into dendritic cells and macrophages and secrete superoxide, myeloperoxidase, and cytokines the regulate both local and systemic inflammatory responses[20,21]. A previous study by Kitaya et al.[22] demonstrated aberrant endometrial expression of several B-cell extravasation-associated proinflammatory proteins in patients with CE. The endometrium

Characteristic	Total (n = 631)	CD138 negative	CD138 positive	*P*-value
		n = 137	n = 494	
Age, Mean ± SD	32.5 ± 4.7	32.4 ± 5.0	32.6 ± 4.6	0.722
Gravidity, Mean ± SD	1.1 ± 1.3	1.2 ± 1.2	1.1 ± 1.3	0.472
Parity, Mean ± SD	0.3 ± 0.5	0.3 ± 0.5	0.3 ± 0.5	0.739
Phase, n (%)				0.002
Follicular	547 (86.7)	107 (78.1)	440 (89.1)	
Middle	14 (2.2)	7 (5.1)	7 (1.4)	
Luteal	70 (11.1)	23 (16.8)	47 (9.5)	
Polyp, n (%)	22 (3.5)	2 (1.5)	20 (4)	0.191
Hyperplasia polyp, n (%)	67 (10.6)	5 (3.6)	62 (12.6)	0.003
Hyperplasia, n (%)	2 (0.3)	0 (0)	2 (0.4)	1
Eutocia, n (%)	94 (14.9)	19 (13.9)	75 (15.2)	0.702
Caesarean, n (%)	75 (11.9)	20 (14.6)	55 (11.1)	0.268
History of abortion				
Induction of labor, n (%)	28 (4.4)	7 (5.1)	21 (4.3)	0.666
Medical, n (%)	12 (1.9)	2 (1.5)	10 (2)	1
Artificial, n (%)	97 (15.4)	21 (15.3)	76 (15.4)	0.987
Curettage, n (%)	102 (16.2)	27 (19.7)	75 (15.2)	0.203
Spontaneous, n (%)	40 (6.3)	8 (5.8)	32 (6.5)	0.786
Inevitable abortion, n (%)	4 (0.6)	0 (0)	4 (0.8)	0.582
Habitual, n (%)	29 (4.6)	8 (5.8)	21 (4.3)	0.432
Ectopic history, n (%)				0.497
No	541 (85.7)	115 (83.9)	426 (86.2)	
Yes	90 (14.3)	22 (16.1)	68 (13.8)	
Causes of infertility				
Primary, n (%)	57 (9.0)	13 (9.5)	44 (8.9)	0.833
Chromosome, n (%)	32 (5.1)	7 (5.1)	25 (5.1)	0.982
Ovarian, n (%)	42 (6.7)	13 (9.5)	29 (5.9)	0.133
PCOS, n (%)	80 (12.7)	17 (12.4)	63 (12.8)	0.915
Fallopian, n (%)	155 (24.6)	32 (23.4)	123 (24.9)	0.711
Endometriosis, n (%)	28 (4.4)	8 (5.8)	20 (4)	0.368
Pelvic inflammatory disease, n (%)	110 (17.4)	27 (19.7)	83 (16.8)	0.428
Male, n (%)	81 (12.8)	14 (10.2)	67 (13.6)	0.301
Disfavorable pregnancy, n (%)	125 (19.8)	31 (22.6)	94 (19)	0.35
UU infection histroy, n (%)	190 (32.6)	46 (37.4)	144 (31.4)	0.206
Laboratory inspection				
WBC, Mean ± SD	6.3 ± 1.5	6.2 ± 1.6	6.4 ± 1.5	0.415
NEUT, Mean ± SD	3.8 ± 1.2	3.7 ± 1.2	3.8 ± 1.2	0.396
%NEUT, Mean ± SD	58.5 ± 9.3	58.1 ± 8.9	58.7 ± 9.4	0.54
MONO, Mean ± SD	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.191
%MONO, Mean ± SD	5.9 ± 1.5	6.2 ± 1.8	5.8 ± 1.4	0.008
LYMPH, Mean ± SD	2.1 ± 0.6	2.0 ± 0.6	2.1 ± 0.6	0.477
%LYMPH, Mean ± SD	33.4 ± 8.0	33.3 ± 8.3	33.4 ± 7.9	0.943
PLT, Mean ± SD	275.5 ± 63.7	262.1 ± 68.7	279.3 ± 61.8	0.005

Table 1. Baseline characteristics of the study participants. Middle, late follicular and early luteal; PCOS, polycystic ovary syndrome; UU, ureaplasma urealyticum; WBC, white blood cell; NEUT, neutrophilic granulocyte; %NEUT, neutrophilic granulocyte percentage; MONO, monocyte; %MONO, monocyte percentage; LYMPH, lymphocyte; %LYMPH, lymphocyte percentage; PLT, platelets.

is infiltrated by various mononuclear immune cells, including macrophages, cytotoxic T (Tc) cells, and NK cells, whose proportions fluctuate during the menstrual cycle[23]. These immune cells also play essential roles in the physiological processes of reproductive organs, such as trophoblast invasion and mucosal angiogenesis[24]. According to Cicinelli et al.[25], genes involved in cell proliferation, inflam[1]mation, and apoptosis—such as those encoding epidermal growth factor (EGF), vascular endothelial growth factors A, B, and C (VEGF-A, -B, -C), cyclins B1 and D3, cell division control protein variants, interferon-γ, interleukin-12, tumor necrosis factor,

Characteristic	OR (95% CI)	*P*-value
Age (years)	1.01 (0.97 ~ 1.05)	0.722
Gravidity	0.95 (0.82 ~ 1.1)	0.471
Parity	0.94 (0.65 ~ 1.35)	0.738
Eutocia, n (%)	1.11 (0.65 ~ 1.91)	0.703
Caesarean, n (%)	0.73 (0.42 ~ 1.27)	0.269
Follicular	2.28 (1.39 ~ 3.74)	0.001
Middle	0.27 (0.09 ~ 0.77)	0.015
Luteal	0.52 (0.3 ~ 0.89)	0.018
Polyp, n (%)	2.85 (0.66 ~ 12.34)	0.162
Hyperplasia polyp, n (%)	3.79 (1.49 ~ 9.62)	0.005
Hyperplasia, n (%)	589,818.41 (0 ~ Inf)	0.983
Induction of labor, n (%)	0.82 (0.34 ~ 1.98)	0.666
Medical, n (%)	1.39 (0.3 ~ 6.44)	0.67
Artificial, n (%)	1 (0.59 ~ 1.7)	0.987
Curettage, n (%)	0.73 (0.45 ~ 1.19)	0.204
Spontaneous, n (%)	1.12 (0.5 ~ 2.48)	0.786
Inevitable abortion, n (%)	592,225.83 (0 ~ Inf)	0.976
Habitual, n (%)	0.72 (0.31 ~ 1.65)	0.434
Ectopic history, n (%)	0.83 (0.49 ~ 1.41)	0.497
Primary, n (%)	0.99 (0.42 ~ 2.34)	0.982
Chromosome, n (%)	0.59 (0.3 ~ 1.18)	0.136
Ovarian, n (%)	1.03 (0.58 ~ 1.83)	0.915
PCOS, n (%)	1.09 (0.7 ~ 1.7)	0.711
Fallopian, n (%)	0.68 (0.29 ~ 1.58)	0.37
Endometriosis, n (%)	0.82 (0.51 ~ 1.33)	0.428
Pelvic inflammatory disease, n (%)	0.93 (0.49 ~ 1.79)	0.833
Male, n (%)	1.38 (0.75 ~ 2.54)	0.302
Disfavorable pregnancy, n (%)	0.8 (0.51 ~ 1.27)	0.35
UU infection histroy, n (%)	0.77 (0.51 ~ 1.16)	0.206
WBC	1.05 (0.93 ~ 1.19)	0.415
NEUT	1.07 (0.92 ~ 1.25)	0.395
%NEUT	1.01 (0.99 ~ 1.03)	0.539
MONO	0.35 (0.07 ~ 1.69)	0.191
%MONO	0.85 (0.76 ~ 0.96)	0.009
LYMPH	1.13 (0.81 ~ 1.57)	0.477
%LYMPH	1 (0.98 ~ 1.02)	0.943
PLT	1 (1 ~ 1.01)	0.006

Table 2. Univariate analysis for the presence of CE positive. OR, odds ratio; CI, confdence interval; PCOS, polycystic ovary syndrome; UU, ureaplasma urealyticum; WBC, white blood cell; NEUT, neutrophilic granulocyte; %NEUT, neutrophilic granulocyte percentage; MONO, monocyte; %MONO, monocyte percentage; LYMPH, lymphocyte; %LYMPH, lymphocyte percentage; PLT, platelets.

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
%MONO	0.85 (0.76 ~ 0.96)	0.009	0.85 (0.75 ~ 0.96)	0.007	0.84 (0.75 ~ 0.96)	0.007	0.84 (0.74 ~ 0.95)	0.006	0.83 (0.72 ~ 0.95)	0.007	0.82 (0.71 ~ 0.95)	0.01

Table 3. Multivariate logistical regression for MP and the presence of CE positive. Model 1 was unadjusted; Model 2 was adjusted for age,gravidity, parity; Model 3 was adjusted for model 2 plus follicular, middle, luteal; Model 4 was adjusted for model 3 plus polyp, hyperplasia polyp, hyperplasia; Model 5 was adjusted for model 4 plus induction of labor, medical abortion, artificial, curettage, spontaneous abortion,inevitable, habitual, ectopic, primary, chromosome, ovarian, PCOS, fallopian, endometriosis, pelvic inflammatory disease, male, disfavorable pregnancy, UU infection histroy; Model 6 was adjusted for model 5 plus NEUT, LYMPH, PLT.

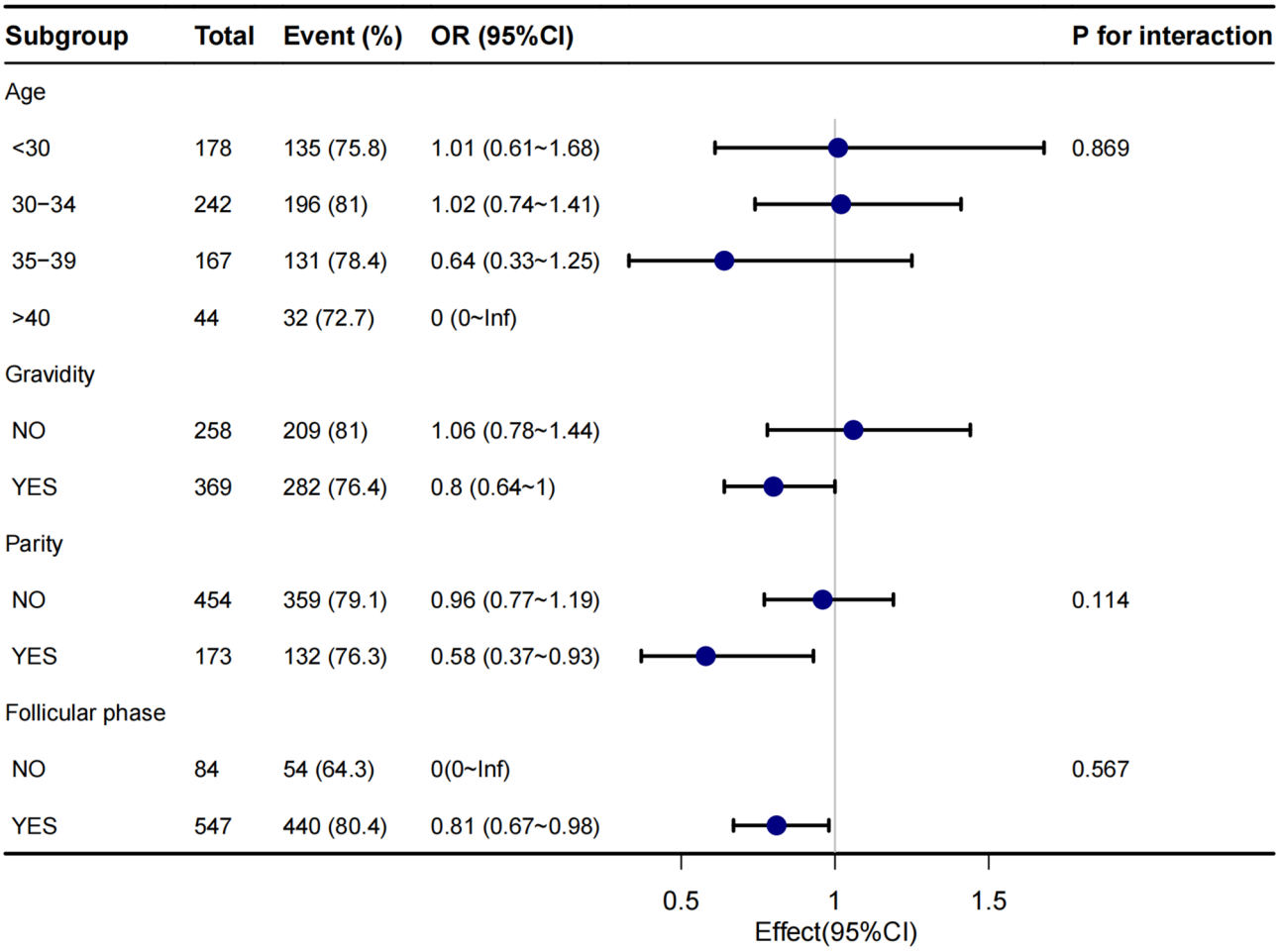

Fig. 2. Association between MP and CE positive. Each stratification was adjusted for age, Gravidity, Parity, follicular, middle, luteal, polyp, hyperplasia polyp, hyperplasia, Induction of labor, Medical abortion, artificial, Curettage, Spontaneous abortion, Inevitable, Habitual, Ectopic, Primary, Chromosome, Ovarian, PCOS, Fallopian, Endometriosis, Pelvic inflammatory disease, Male, Disfavorable pregnancy, UU infection histroy, NEUT, LYMPH, PLT.

Analysis	Total	Event (%)	Adjusted OR (95% CI)	*P* value
Excluding participants endometrial abnomality	540	410 (75.9)	0.83 (0.71 ~ 0.96)	0.015
Excluding non-follicular Phase	547	440 (80.4)	0.78 (0.66 ~ 0.92)	0.003
Excluding participants endometrial abnomality and non-follicular Phase	468	366 (78.2)	0.82 (0.7 ~ 0.95)	0.011

Table 4. Sensitivity analyses. Each stratification was adjusted for age, Gravidity, Parity, follicular, middle, luteal, polyp, hyperplasia polyp, hyperplasia, Induction of labor, Medical abortion, artificial, Curettage, Spontaneous abortion, Inevitable, Habitual, Ectopic, Primary, Chromosome, Ovarian, PCOS, Fallopian, Endometriosis, Pelvic inflammatory disease, Male, Disfavorable pregnancy, UU infection histroy, NEUT, LYMPH, PLT.

transforming growth factor β1, BCL-2-associated X protein (BAX) transcript variant alpha—were differentially expressed in the endometrium of women with CE compared with their healthy counterparts.

We propose that this inverse correlation may be attributed to the reciprocal regulation between monocyte and plasma cell functions within the local immune microenvironment of CE. Monocytes, as key components of the innate immune system, are recruited to the endometrium during the early stages of inflammation, where they phagocytose pathogens and secrete pro-inflammatory cytokines (e.g., TNF-α, IL-6) to initiate immune responses. As CE progresses, monocytes differentiate into macrophages and further regulate B lymphocyte activation and differentiation through cytokines such as IL-10 and TGF-β. When B lymphocytes differentiate into plasma cells—the principal effector cells of humoral immunity— producing antibodies against persistent pathogens, the number of recruited monocytes and macrophages may gradually decrease, either due diminished

pro-inflammatory signaling or clearance after completing the initial immune activation. This dynamic transition from innate to adaptive immune response may account for the inverse density correlation observed in this study.

MP assay holds unique clinical significance for CE diagnosis in infertile patients and provides supplementary value to the gold-standard plasma cell assay (e.g., CD138 IHC).

Early screening advantage: Plasma cell infiltration typically indicates a relatively advanced stage of chronic inflammation, whereas monocyte elevation may occur earlier (as an initial innate immune response) in subclinical CE. This enables earlier identification of patients at risk of developing overt CE, particularly in asymptomatic infertile women.

Technical accessibility: Unlike plasma cell detection (which requires invasive endometrial biopsy and IHC staining), MP can be measured through routine peripheral blood tests (e.g., complete blood count with differential). It is noninvasive, low cost, and well accepted by patients, facilitating large-scale preliminary screening.

Prognostic implications: Beyond diagnosis, MP may reflect CE activity. Elevated monocyte levels may indicate ongoing inflammation—even when plasma cell density is low—potentially prompting more aggressive anti-inflammatory interventions. Conversely, normalized post-treatment monocyte levels could serve as a non-invasive indicator of therapeutic response, offering an advantage over plasma cell assays, which primarily confirm the presence of chronic inflammation.

Histological analysis for CD138 positivity can greatly facilitate the identification of CE cases. According to the literature, the incidence of CE generally ranges from 3 to 60%[26], which can be attributed to the varied diagnostic criteria applied in histological examinations across studies. Higher CE incidences have also been reported. For instance, a single-center study reported a CE incidence of 72% among females with suspected pelvic inflammatory disease[27]. We observed herein an even higher CE incidence of 78% among infertile patients. This high incidence may result from the introduction of CD138 staining in disease diagnosis or may simply reflect characteristics of the study cohort. Therefore, we speculate that discrepancies in CE incidence among studies can be ascribed to differences in diagnostic criteria and cohort heterogeneity.

Our pathological analysis revealed that 547, 14, and 70 participants were in the follicular, late follicular/early luteal, and luteal phases, respectively, accounting for 86.7%, 2.2%, and 11.1% of the total cohort ($P=0.002$). Additionally, the proportion of patients with CE among infertile individuals was higher in the follicular phase (80%) than in the luteal phase (67%). These results are consistent with two previous studies, which reported that 26%[17] and 60%[28] of participants were in the follicular phase, whereas 18% and 20% were in the luteal phase.

In our analysis, age, cesarean delivery, history of abortion, ectopic pregnancy history, and causes of infertility were not associated with the risk of CE, corroborating the conclusions of Kitaya et al.[29,30]. No relationship was observed between cervical UU infection before hysteroscopy and CE. Cicinelli et al.[31] reported that in patients with CE, the microorganisms isolated from endometrial tissue cultures differed from those identified in endocervical or vaginal swab cultures.

The correlation between endometrial polyps and CE (OR = 2.85; 95% CI 0.66–12.34; $P=0.162$) did not reach statistical significant in our study. Kitaya et al.[30] failed to detect plasma cell infiltration within specimens from endometrial polyps (EPs). However, some investigations have demonstrated a correlation between CE and EPs[32,33]. For example, Cicinelli et al.[34] reported a higher incidence of CE in females with CD138-positive EPs than in those with CD138-negative EPs (64.1% vs. 30.7%; $P<0.0001$). This discrepancy may stem from the small sample size of females with EPs (n = 22) in our study. In our study, there was a high incidence of CE among participants with endometrial polypoid hyperplasia (OR = 3.79; 95% CI 1.49–9.62; $P=0.005$). Cicinelli et al. have shown in several of their studies that the presence of endometrial micro-polyps at hysteroscopy may be a reliable feature for diagnosing CE[32,33], with the severity of histological abnormalities correlating with hysteroscopic findings[34]. In a descriptive histological study using endometrial samples from 435 infertile patients, Carvalho et al.[35] reported that 70% of vascular alterations in CE corresponded to vessel wall hyaline thickening, showing morphology similar to that of the thick-walled vessels along the vascular axis of EPs. Thus, one possible explanation for this result is that vascular alterations in CE may have influenced the pathologists.

Our study demonstrated a significant inverse correlation between peripheral blood monocyte percentage and endometrial plasma cell density. Although the precise immunological mechanisms within the endometrium require further investigation, several plausible explanations can be proposed based on established immunological principles and observations of chronic inflammation. Future research should include in-depth mechanistic studies using flow cytometry and functional assays, prospective multicenter validation of diagnostic performance, and the establishment of clinical cutoff values. Additionally, exploration of multi-marker panels that combine MP with other biomarkers may further enhance diagnostic and prognostic utility. Critical assessment of the biomarker's ability to predict treatment response and, crucially, fertility outcomes; investigation of links to specific endometrial pathogens or microbiome profiles; and research into standardization and automation for clinical implementation. We believe these proposed directions provide a clear roadmap for building upon the foundations laid by this retrospective study and ultimately translating the findings into improved clinical management of chronic endometritis in infertile patients.

Limitations

Our study has certain limitations. First, the single-center and cross-sectional nature of this research may limit the generalizability of our findings. Although MP has been correlated with CE incidence, the temporal association between the two remains to be determined and warrants further subtly-designed cohort investigations. Second, the endometrial biopsy specimens we obtained for downstream analyses may not faithfully reflect the actual status of the whole endometrium, although we tried to collect as many first biopsy samples as possible within the defined time frame. Lastly and most importantly, the implications of our findings for pregnancy outcomes warrant further investigation to better clarify their clinical significance and application value.

Conclusions

The results of our study indicate that MP is inversely correlated with CE incidence among infertile patients. Because MP can be readily obtained from routine complete blood count tests, it has potential as an early predictive marker for CE. Future studies ae warranted to elucidate the underlying the mechanisms linking MP and CE.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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