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REVIEW ARTICLE

Infectious endometritis: systematic analysis of risk factors, clinical manifestations, and treatment strategies

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ABSTRACT

Introduction: infectious endometritis is an inflammation of the endometrium caused by aerobic and anaerobic microorganisms, with significant impact on female reproductive health. **Objective:** to analyze risk factors, clinical manifestations, and therapeutic strategies for infectious endometritis through a systematic literature review.
Methods: a systematic review of the scientific literature was conducted across multiple databases. The search employed an algorithm combining keywords and Boolean operators to identify relevant sources. Selected studies, after applying inclusion and exclusion criteria, were critically analyzed considering recency, methodological quality, and thematic relevance, and integrated into the final synthesis of the review.
Development: reviewed studies identify sexually transmitted infections, cesarean delivery, abortions, and invasive gynecological procedures as key risk factors. Diagnosis relies on clinical assessment, laboratory tests, and ultrasound, with hallmark signs including fever, uterine tenderness, and abnormal lochia. Acute cases require intravenous antibiotics followed by oral therapy, while chronic endometritis demands prolonged, culture-guided regimens. Doxycycline and combinations with metronidazole or ciprofloxacin show efficacy. Prevention focuses on appropriate STI management and sterile techniques during obstetric procedures.
Conclusions: infectious endometritis can be prevented and effectively treated through early diagnosis and personalized therapies. Pathogen diversity necessitates tailored approaches and standardized protocols. Longitudinal studies evaluating reproductive outcomes and optimizing public health prevention are needed.

Keywords: Diagnosis; Endometritis; Risk Factors; Reproductive Health; Therapeutics.

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INTRODUCTION

Infectious endometritis is an inflammation of the endometrium caused by various aerobic and anaerobic microorganisms and represents a significant issue in female reproductive health. Its clinical impact is reflected in complications affecting patients' quality of life and the potential for severe sequelae if not diagnosed and treated promptly. Scientific literature has documented its prevalence and etiology, emphasizing the need for accurate diagnostic strategies and effective therapies to reduce the burden of this condition in gynecological practice. [1,2,3]

Despite advances in understanding endometritis, gaps remain regarding specific infection mechanisms and optimal prevention and treatment practices. Risk factors such as cesarean delivery, inadequate prenatal care, and prior genitourinary tract infections have been identified as key determinants. However, available research presents methodological limitations and difficulties in generalizing findings due to heterogeneity in studied populations and variability in research designs. [4,5,6]

In this context, a systematic bibliographic review integrating and critically analyzing existing evidence on infectious endometritis is warranted. This approach will allow identification of major risk factors, description of key clinical manifestations, and evaluation of therapeutic strategies proposed in recent literature.[7,8] It will also help recognize current limitations and highlight priority areas for future research to optimize prevention, diagnosis, and treatment of this pathology for the benefit of women's reproductive health.[9,10] Given these considerations, this review was conducted with the objective of analyzing risk factors, clinical manifestations, and therapeutic strategies for infectious endometritis through a systematic literature review.

METHODS

This study was structured as a systematic literature review following PRISMA guidelines. The search period spanned from 2010 to 2024 to include recent studies on risk factors, clinical manifestations, and treatment strategies for infectious endometritis. Databases consulted included PubMed, Scopus, SciELO, MEDLINE, Google Scholar, and ResearchGate, along with grey literature and secondary references.

The search strategy employed Health Sciences Descriptors (DeCS) and Boolean operators such as "endometritis" OR "infectious endometritis" AND "risk factors" OR "clinical manifestations" AND "treatment." Articles in Spanish and English were included to ensure a broad, multilingual perspective.

Inclusion criteria encompassed studies published within the defined timeframe, original research, systematic reviews, and meta-analyses directly addressing infectious endometritis. Duplicates, articles without full access, irrelevant studies, and publications outside the temporal range were excluded.

The selection process occurred in several phases: record identification, title and abstract screening, and full-text analysis. Initially, 65 records were obtained; 30 were excluded based on criteria, and 20 underwent full-text evaluation. Finally, 15 articles met inclusion criteria and were incorporated into the analysis. The procedure was represented using a PRISMA flow diagram (Figure 1), illustrating identification, screening, eligibility, and inclusion stages.

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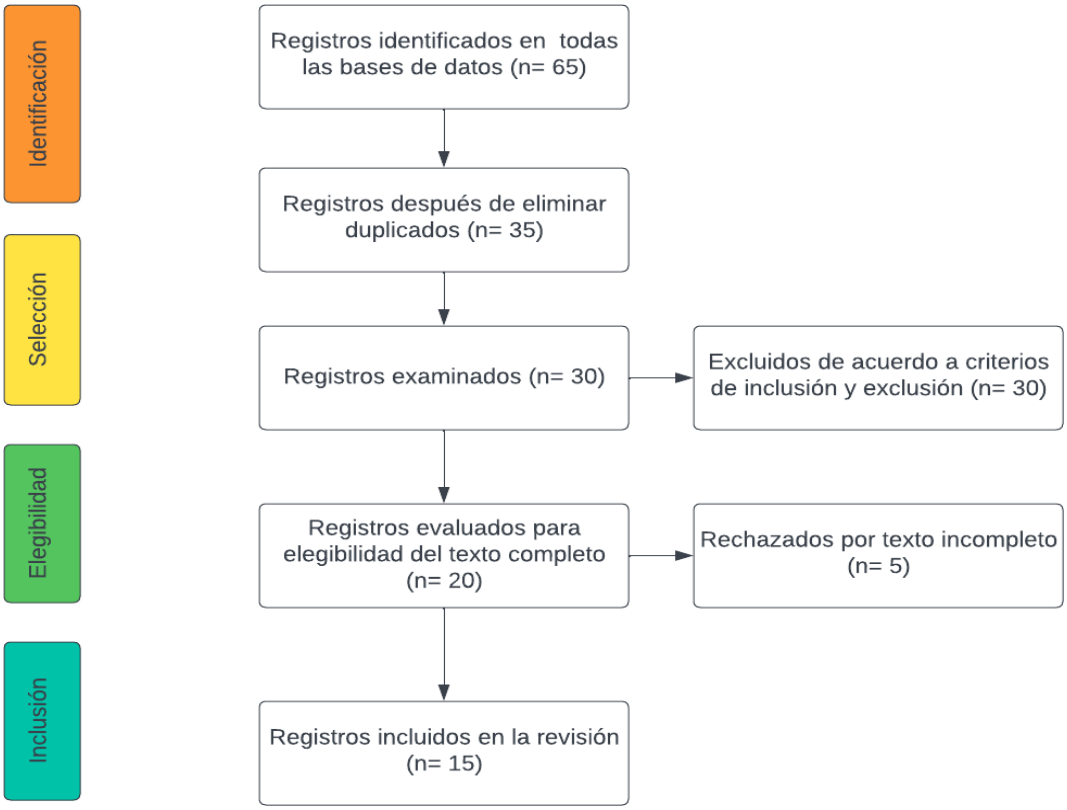

Fig. 1 Screening flowchart

Data extraction and analysis focused on key variables such as author, year, methodological design, study population, intervention type, and main outcomes. Synthesis was qualitative, integrating findings on etiology, diagnosis, treatment, and prevention of infectious endometritis. No meta-analysis was performed due to study heterogeneity, although consistent trends emerged supporting the importance of early diagnosis and personalized treatment.

DEVELOPMENT

Endometritis refers to a broad spectrum of infections specifically affecting the endometrial lining, myometrium, and parametrium. Likely causative agents include aerobic microorganisms such as Group A, B, and D *Streptococcus*, *Enterococcus*, Gram-negative bacteria (*E. coli*, *Klebsiella*, *Proteus* spp.), *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Gardnerella vaginalis*. Anaerobes include *Peptococcus* and *Peptostreptococcus* species, *Bacteroides fragilis* group, *Prevotella* spp., *Clostridium*, *Fusobacterium*, *Mobiluncus* spp., and *Mycoplasma* species.[11]

Risk factors associated with predisposition to infectious endometritis include sociodemographic variables, particularly maternal age under 19 or over 35 years. Additional factors involve antepartum conditions such as inadequate prenatal care (fewer than six visits) and pregnancy-related pathologies like anemia, premature rupture of membranes, and urinary tract infection. Intrapartum risks include cesarean delivery, ≥4 vaginal examinations, manual placental removal, and postpartum uterine cavity exploration.[12]

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The mechanism of uterine invasion depends on delivery route and aforementioned risk factors. Cesarean section is associated with necrotic tissue formation and bacterial proliferation due to surgical wound dehiscence, suture necrosis, and hematomas. Vaginal deliveries—though less prevalent—primarily involve ascending genitourinary pathogens with concomitant superinfection. Additional contributing factors include excessive manipulation, foreign bodies, and episiotomy.[13]

Diagnosis of infectious endometritis is primarily clinical, based on patient history, clinical manifestations, physical examination, and risk factors. When suspicion arises or severity assessment is needed, imaging and laboratory methods are highly useful.[14]

As previously noted, clinical diagnosis is confirmed by the presence of fever (>38°C in two readings 6 hours apart), typically on postpartum days 3–5, accompanied by:[8,10,11]
• Uterine tenderness
• Uterine subinvolution (inadequate retraction)
• Foul-smelling or turbid lochia

Diagnostic investigations include total leukocyte count, endocervical swab culture, and microscopic vaginal discharge examination. In non-responsive cases, pelvic abscess may develop, requiring laparoscopic drainage followed by postoperative intravenous antibiotic therapy. Ultrasound aids diagnosis in postpartum patients with abdominal pain and fever, revealing thickened heterogeneous endometrium, fluid collection, and intrauterine air foci.[15]

Accurate differential diagnosis is vital to exclude conditions with similar symptoms. Urinary tract infection may present with dysuria and abdominal discomfort. Surgical wound infection manifests with fever, erythema, swelling, purulent drainage, and incisional pain. Postpartum hemorrhage causes fever and abdominal pain but is distinguished by blood loss. Uterine subinvolution—failure of the uterus to return to normal size—presents with pain and discomfort.[16]

Additionally, ectopic pregnancy or spontaneous abortion may cause abdominal pain and bleeding, usually with recent pregnancy history. Pelvic inflammatory disease (PID) presents with abdominal pain and fever linked to reproductive organ infections. Adenomyosis or uterine fibroids cause pain and bleeding but not necessarily fever. Comprehensive clinical evaluation—including history, physical exam, laboratory tests, and imaging—is essential to differentiate these conditions from infectious endometritis.[16]

Treatment differs according to the two main types: acute and chronic endometritis.

➢ Acute Endometritis Treatment

Beyond symptomatic management, immediate bed rest, adequate hydration, and intravenous antibiotics for the first 48 hours are required in severe cases, followed by oral antibiotics. For mild-to-moderate disease, oral antibiotics alone suffice. Sexual partners should also be treated, and barrier contraception counseling provided.[17]

Acute endometritis treatment requires broad-spectrum coverage against likely pathogens and should begin as early as possible to prevent long-term complications. Regimen selection depends on availability, acceptability, and cost. For mild-to-moderate PID, parenteral and oral regimens are equally effective. Hospitalization is indicated when associated with:
• Acute abdomen (surgical emergency)
• Pelvic abscess
• PID during pregnancy

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- High fever
- Severe nausea/vomiting
- Non-adherence to oral therapy
- Lack of improvement with oral antibiotics

Oral medications may generally be initiated 24–48 hours after clinical improvement. Tubo-ovarian abscess mandates hospitalization and observation for at least 24 hours.[17,18]

CDC 2015-recommended parenteral regimens include:[1,19]
- Cefotetan 2 g IV twice daily or cefoxitin 2 g IV four times daily plus doxycycline 100 mg orally twice daily
- Doxycycline 100 mg orally twice daily is continued for 14 days after 24–48 hours of clinical improvement
- IV clindamycin 900 mg every 8 hours plus gentamicin IV loading dose (2 mg/kg) followed by maintenance (1.5 mg/kg every 8 hours) or single daily dose (3–5 mg/kg)
- Oral clindamycin 450 mg four times daily or doxycycline 100 mg twice daily to complete 14-day therapy

Oral or intramuscular treatment is recommended for mild-to-moderate acute PID, especially in low-resource settings. Parenteral and oral regimens yield equivalent outcomes in mild-to-moderate PID. Patients failing oral/IM therapy within 72 hours require reevaluation and IV therapy.[17,20] Recommended regimens:

- Single IM ceftriaxone 250 mg plus doxycycline 100 mg twice daily ± metronidazole 500 mg twice daily for 14 days
- Single IM cefoxitin 2 g plus oral probenecid 1 g plus doxycycline 100 mg twice daily ± metronidazole 500 mg twice daily for 14 days
- Third-generation cephalosporin IM plus doxycycline 100 mg twice daily ± metronidazole 500 mg twice daily for 14 days

➢ Chronic Endometritis Treatment

Chronic endometritis treatment is primarily oral antibiotic-based, guided by endometrial aspiration/biopsy culture and Gram stain; endometrial aspiration is repeated post-treatment. No standard regimen exists. Various antibiotics and doses have been prescribed, with endometrial receptivity improving after antibiotic therapy. First-line regimen: doxycycline 100 mg twice daily for 14 days. Second-line options include ciprofloxacin and metronidazole 500 mg once daily for two weeks or ofloxacin 400 mg once daily and metronidazole 500 mg once daily for two weeks.[3,6,17]

Specific antibiotic regimens have been described for infertile patients with chronic endometritis based on microbiological profiles. Patients with Gram-negative and Gram-positive bacteria received ciprofloxacin 500 mg twice daily for 10 days plus amoxicillin-clavulanate 2 g once daily for 8 days. Those with *Mycoplasma* or *Ureaplasma* received josamycin 2 g/day for 12 days; resistant cases received minocycline 200 mg/day for 12 days.[4,9,10]

Chronic endometritis persisted in 25 % of patients after three courses of oral antibiotic therapy, indicating reasonable efficacy. Patients with persistent chronic endometritis received intrauterine antibiotic infusion. Two of three reported ongoing pregnancies without complications at 19 and 20 weeks. Animal models showed reduced uterine microbial load and enhanced local immune defense with intrauterine antibiotic infusion, resulting in endometrial restoration.[6,17]

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The World Health Organization (WHO) recommends short-course directly observed treatment (DOTS) as the preferred approach. Four drugs are administered: isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) for two months (HRZE), followed by H, R, and E (HRE) daily for four months. Daily treatment is directly supervised. A 60-kg adult receives: isoniazid 300 mg/day, rifampicin 600 mg/day, pyrazinamide 1600 mg/day, and ethambutol 1200 mg/day. Combined kits may also be prescribed without direct supervision (non-DOTS).[1,5,19]

Antitubercular therapy effects on the endometrium of women with genital tuberculosis showed restored regular menstrual cycles. Histopathology revealed disappearance of epithelioid granulomas and acid-fast bacilli (AFB). Ultrasound showed endometrial thickness improvement from 7 mm to 7,5 mm. Hysteroscopy revealed improved uterine cavity appearance post-treatment. Intrauterine adhesions/Asherman syndrome prevalence decreased from 62 % pre-treatment to 28,7 % post-treatment. Grade I adhesions improved significantly (34 % to 2,1 %, $p<0,001$), but higher-grade adhesions showed no improvement. Thus, early detection of tuberculous endometritis is crucial. Early antitubercular therapy improved menstrual cycles, endometrial thickness, and reduced grade I adhesion incidence—suggesting potential reproductive outcome benefits.[8,17,21]

Prevention of Endometritis

Endometritis is largely preventable through early detection and management of sexually transmitted infections (STIs), safer sexual practices, and sterile techniques during pelvic procedures (vaginal delivery, cesarean section, abortions).[2,6,17] Cesarean delivery in the second stage of labor is associated with higher endometritis rates. Reducing ascending infection via vaginal bacterial load reduction—using antiseptic vaginal preparations—is a plausible mechanism for endometritis prevention.[20]

Povidone-iodine vaginal preparation reduces vaginal organisms by >95 %. Although high-alcohol chlorhexidine formulations may be caustic, low-dose chlorhexidine preparations exist. Since vaginal bacteria must ascend through the hysterotomy site to cause subcutaneous infection, wound infection prevention via vaginal antisepsis may not be an appropriate outcome measure.[12]

The WHO technical consultation adopted 20 recommendations covering priority issues in peripartum maternal infection prevention and treatment. Preventive measures include avoiding routine minor procedures (e.g., pubic/perineal shaving), antimicrobials for vaginal and cesarean delivery, and antibiotic prophylaxis for obstetric conditions/procedures posing infection risk (premature rupture of membranes, meconium-stained amniotic fluid, perineal lacerations, manual placental removal, instrumental vaginal delivery, cesarean section). [1,2,3]

The etiology of infectious endometritis involves diverse aerobic and anaerobic microorganisms—including *Streptococcus*, *Staphylococcus*, *E. coli*, and *Gardnerella vaginalis*—consistent with prior studies identifying these as common causative agents. Pathogen diversity underscores the importance of precise causal agent identification for effective treatment.[11]

Sociodemographic and obstetric risk factors—such as maternal age, inadequate prenatal care, and delivery complications like cesarean section—are associated with increased endometritis predisposition. This highlights the need for adequate prenatal care and preventive measures during delivery to minimize risk, consistent with research emphasizing prenatal care's role in preventing puerperal infections.[14]

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Clinical diagnosis—based on fever, uterine tenderness, and abnormal lochia—remains widely accepted. Incorporating laboratory tests and imaging (e.g., ultrasound) is crucial for confirmation and severity assessment. Ultrasound findings—thickened heterogeneous endometrium with fluid accumulation—are indicative of endometritis and align with other researchers' reports.[9,13,15]

Treatment must be tailored to endometritis type. Acute cases respond well to IV antibiotics followed by oral therapy, especially when initiated promptly—consistent with CDC guidelines and studies supporting broad-spectrum antibiotics. Chronic endometritis requires prolonged, culture-guided therapy. Doxycycline and ciprofloxacin-metronidazole combinations show efficacy, as highlighted in both this review and existing literature.[17]

CONCLUSIONS

This review provides an integrative and critical overview of bacterial endometritis, addressing etiology, diagnosis, treatment, and prevention while identifying key risk factors and effective clinical practices based on recent literature. Early diagnosis and adherence to clinical guidelines are emphasized to prevent severe complications, alongside the need for personalized therapies given pathogen diversity. The analysis identifies research gaps—particularly the lack of longitudinal studies evaluating long-term treatment effects. To advance, broader and more heterogeneous studies are recommended, along with exploration of novel prevention strategies, targeted therapies, and advanced technologies for early diagnosis—to optimize bacterial endometritis management and strengthen female reproductive health.

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