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Review Article

Advances in Pelvic Inflammatory Disease (PID): Epidemiology, Pathogenesis and Management

Jiménez-Huerta Juan[1], Vázquez-Cervantes Ashley Georgina[2]*, Morales-Galicia Arnulfo Eduardo[3], Ortiz-Pinzón Brisa Yeretzi[4], Saldivar-Trejo Elizabeth[5]

[1]Chief of the Emergency and Toco-surgical Unit of the Gynecology and Obstetrics Service, Hospital Juárez de México (HJM), Ministry of Health (SS), Mexico
[2]Faculty of Medicine, La Salle University (ULSA), Mexico
3Faculty of Medicine (FACMED), National Autonomous University of Mexico (UNAM), Mexico
[4]Faculty of Medicine, Autonomous University of Guerrero (UAGro), Mexico
[5]School of Medicine, Saint Luke's University, Mexico

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Abstract: Pelvic Inflammatory Disease (PID) is a complex clinical syndrome that affects the female upper genital tract, including endometritis, salpingitis, oophoritis, and tubo-ovarian abscesses. Its etiology is predominantly associated with ascending infections, primarily by Neisseria gonorrhoeae and Chlamydia trachomatis, although in our population, the microbiota has been observed to play a significant role. PID can lead to serious complications such as adhesive syndrome, which can be a determinant of infertility, chronic pelvic pain, and ectopic pregnancy. This article reviews the global and Mexican epidemiology, pathogenic mechanisms, diagnostic criteria, therapeutic approaches, and current preventive strategies, highlighting the importance of early diagnosis and appropriate treatment to minimize long-term sequelae.

Keywords: Pelvic Inflammatory Disease, *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and Infertility.

INTRODUCTION

Pelvic Inflammatory Disease (PID) is one of the most frequent complications of sexually transmitted infections (STIs), constituting a significant threat to female reproductive health. PID encompasses a group of upper genital tract infections including endometritis, salpingitis, oophoritis and tuboovarian abscesses, and is associated with serious consequences such as adhesive syndrome which can be a condition for infertility, chronic pelvic pain and ectopic pregnancy. The prevalence of PID varies globally, with higher rates in countries with limited access to health services and lower awareness of STIs [1]. In Mexico, the incidence of PID remains a major public health problem due to factors such as lack of sex education and limited access to health services [2].

The etiology of PID is multifactorial, mainly involving ascending infections by Neisseria gonorrhoeae and Chlamydia trachomatis. However, a wide range of microorganisms, including anaerobic bacteria and normal vaginal microbiota, may also be involved [3]. The pathogenesis of PID is complex and is mediated by a number of inflammatory mechanisms that can lead to extensive tissue damage and abscess formation.

This article reviews in depth the epidemiology of PID both globally and in Mexico, with a detailed focus on pathophysiology and pathogenesis, as well as available diagnostic and therapeutic methods. Prevention of PID is essential to reduce its long-term impact, and current prevention and management strategies will be discussed.

DEVELOPMENT OF THE TOPIC

EPIDEMIOLOGY

Global Epidemiology

The overall prevalence of PID varies significantly among different regions and populations. The annual incidence of PID is estimated to be approximately 1 million cases in the United States, with similar prevalence in other developed regions [4]. In developing countries, the incidence is generally higher due to the lack of access to health services and STI screening programs [5]. Rates of PID are particularly high in young sexually active women, with a peak incidence between the ages of 15 and 25 years [6].

PID is frequently underdiagnosed because of the nonspecific nature of its symptoms and variability in clinical presentation. Many women with PID present

***Corresponding Author:** Vázquez-Cervantes Ashley Georgina
Faculty of Medicine, La Salle University (ULSA), Mexico

with mild or atypical symptoms, which complicates diagnosis and allows the infection to progress and cause irreversible damage to the reproductive tract [7].

Epidemiology in Mexico

In Mexico, PID is a major health concern, with data revealing an increasing prevalence, especially in young women. According to the National Institute of Statistics and Geography (INEGI), approximately 200,000 cases of PID were reported in 2021, representing a significant increase compared to previous years. Lack of sex education, stigma associated with STIs, and limited access to health services contribute to the high prevalence of PID in the country [8]. According to data from the Ministry of Health, the incidence of PID in Mexico has shown an increase in recent decades, with higher rates in rural areas and among young women [9].

STI screening and treatment programs in Mexico are insufficient, and many women do not receive adequate treatment in a timely manner. This is worsened by the lack of resources and trained personnel in many areas of the country [10].

PATHOPHYSIOLOGY AND PATHOGENESIS

The pathophysiology of PID is complex and multifactorial, involving a dynamic interaction between infectious pathogens and the host immune response. Most cases of PID are caused by ascending infections from the vagina and cervix to the upper genital tract [11].

Infection and Spread

PID is frequently caused by ascending infections of N. gonorrhoeae and C. trachomatis. These bacteria have a remarkable ability to adhere to and penetrate the cervical epithelium, ascending through the upper genital tract and triggering a significant inflammatory response [12].

N. gonorrhoeae produces several surface proteins that facilitate its adherence and invasion of genital tract epithelial cells. The bacterium can evade the immune system by antigenic variation and production of antibody-degrading proteases [13]. Once N. gonorrhoeae reaches the upper genital tract, it elicits a robust neutrophil-mediated inflammatory response, which can lead to abscess formation and tissue damage [14].

C. trachomatis, in contrast, has a unique life cycle that includes an extracellular infectious form (the elementary body) and an intracellular replicative form (the reticulate body). C. trachomatis can evade the host immune response and persist intracellularly, contributing to chronic infections and prolonged tissue damage [15]. The chronic inflammatory response to C. trachomatis infection can result in fibrosis and obstruction of the uterine tubes, leading to infertility [16].

Immune Response and Tissue Damage

The immune response to N. gonorrhoeae and C. trachomatis infection is complex and involves both innate and adaptive immunity. Neutrophils are one of the first immune cell types to respond to infection, releasing a variety of inflammatory mediators that promote bacterial clearance but also cause tissue damage [17].

The production of proinflammatory cytokines, such as IL-1, IL-6, and TNF-α, is a central feature of the immune response to PID. These cytokines contribute to local inflammation and the attraction of more immune cells to the site of infection, exacerbating tissue damage [18]. In addition, the adaptive immune response, mediated by T and B cells, plays a crucial role in clearing the infection, but may also contribute to the pathogenesis of PID through the production of autoantibodies and perpetuation of chronic inflammation (Figure 1) [19].

Vaginal Microbiota and Risk Factors

The vaginal microbiota plays a significant role in susceptibility to PID. The presence of lactobacilli in the normal vaginal microbiota is protective, as these microorganisms produce lactic acid and maintain a low vaginal pH, inhibiting the growth of pathogens [20]. However, vaginal dysbiosis, characterized by a decrease in lactobacilli and an increase in anaerobic bacteria, may predispose to ascending infections and PID [21].

Additional risk factors for PID include intrauterine device (IUD) use, multiple sexual partners, history of STIs, and unprotected sexual practices (Figure 2) [22]. Young age and early sexual activity are also significant risk factors due to immaturity of the cervical epithelium and increased susceptibility to infection [23].

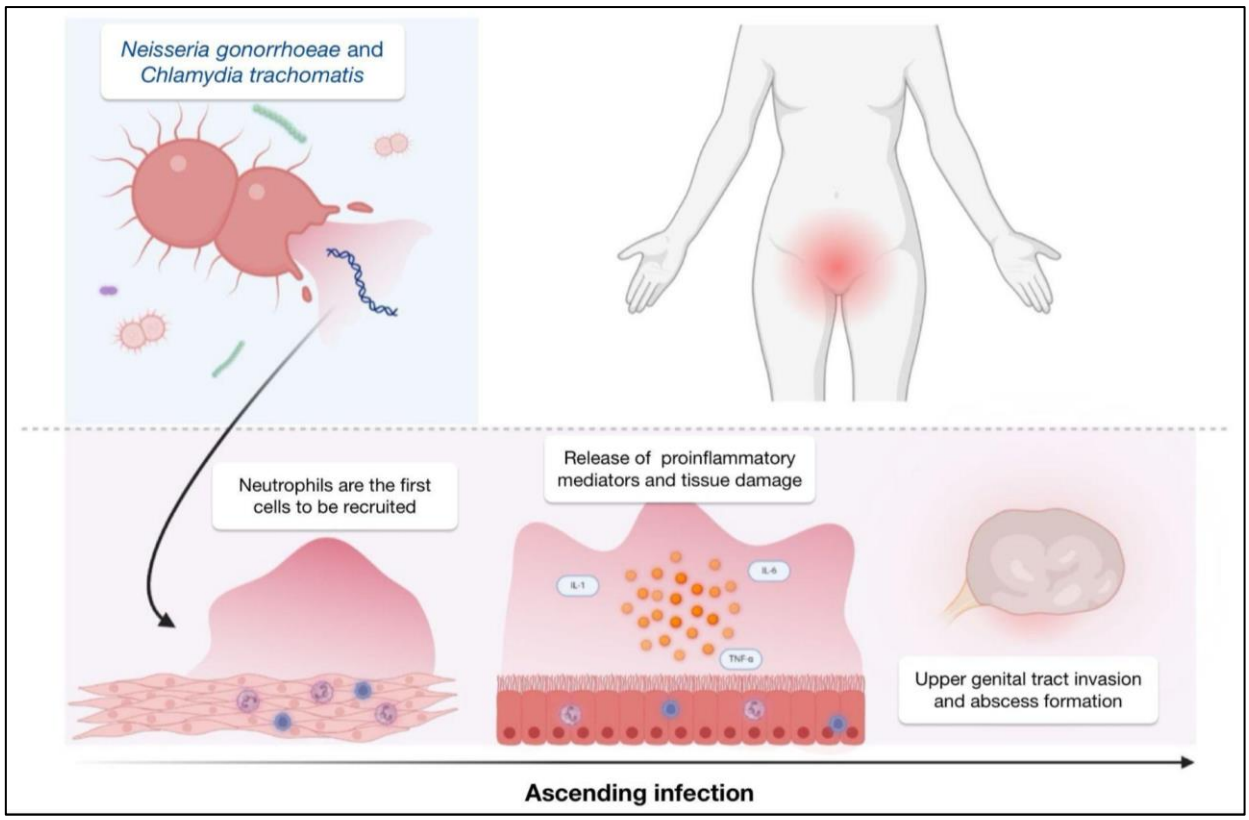

Figure 1: PID begins with gonococcal or chlamydial cervicitis, which generates a dysbiosis of the microbiota, thus originating bacterial vaginosis with overpopulation of pathogenic microorganisms, allowing their ascent to the upper genital tract

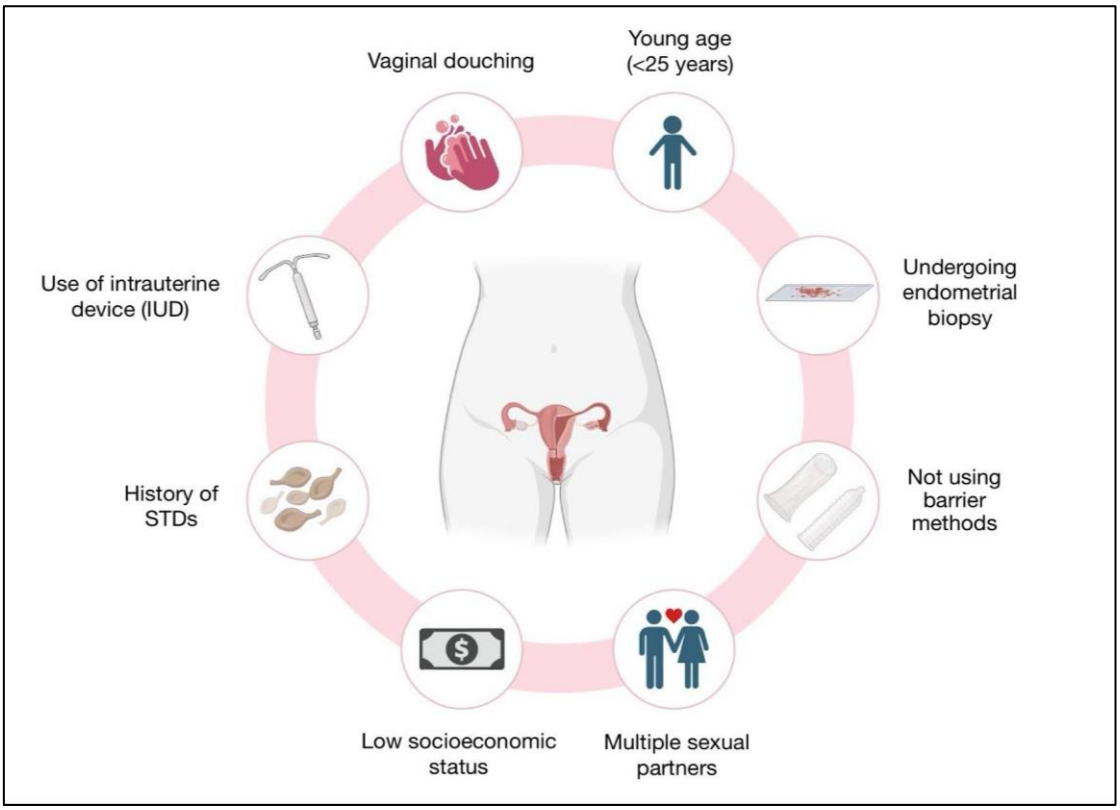

Figure 2: Risk factors include a history of untreated or underdiagnosed sexually transmitted diseases (STDs), prolonged use of intrauterine devices (IUDs), vaginal douching that alters the vaginal microbiota and its environment, young age, endometrial biopsy and history of PID, lack of use of barrier methods, multiple sexual partners, new or existing STDs, and low socioeconomic status

DIAGNOSIS

Diagnosis of PID is challenging due to the variability of clinical presentation and lack of specific tests. Diagnostic criteria include clinical signs, laboratory findings, and imaging studies.

Clinical Criteria and Classification

Clinical signs of PID include pelvic pain, pain on cervical mobilization, and adnexal tenderness. However, these symptoms are nonspecific and may be present in other gynecologic conditions [24]. The presence of fever, leukocytosis and abnormal cervical discharge may also suggest PID (Table 1), but are not diagnostic on their own [25].

MONIF SCALE

Table 1: Pelvic inflammatory disease was classified by Monif in 1982, according to the severity of the clinical findings and the anatomical involvement of the affected structures

GRADE I MILD (not complicated)	**GRADE II** MODERATE (complicated)	**GRADE III** SEVERE
Uncomplicated, without adnexal mass or signs of acute abdomen or peritoneal irritation.	Complicated, presence of adnexal mass or abscess, tubo-ovarian, with or without signs of peritoneal irritation.	Disseminated to extra pelvic structures, ruptured tubo-ovarian abscesses or pelviperitonitis with manifestations of systemic inflammatory response.

Laboratory Testing

Laboratory testing for PID includes detection of specific pathogens by nucleic acid amplification tests (NAATs). These tests are highly sensitive and specific for the detection of N. gonorrhoeae and C. trachomatis [26]. In addition, bacterial cultures and sensitivity tests can be performed to guide antibiotic treatment.

Inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), can support the diagnosis but are not specific for PID [27]. Imaging studies, such as pelvic ultrasound and MRI, may be helpful in identifying the extent of inflammation and the presence of tuboovarian abscesses [28].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of PID includes other conditions that cause acute pelvic pain, such as appendicitis, ovarian torsion, ectopic pregnancy, and gastrointestinal disease [29]. Laparoscopy can be used in complex cases to confirm the diagnosis and exclude other pathologies.

THERAPEUTIC MANAGEMENT

Treatment of PID is oriented towards eradication of infectious pathogens and mitigation of inflammation. Therapeutic management includes the use of antibiotics, pain treatment and, in some cases, surgical interventions.

Antibiotic Therapy

Recommended antibiotic regimens for PID include combinations of ceftriaxone, doxycycline and metronidazole to cover both typical pathogens and anaerobic flora. Treatment should be initiated empirically in patients with suspected PID because of the risk of serious complications if not treated promptly.

In severe or complicated cases, hospitalization and administration of parenteral antibiotics may be necessary. Intravenous antibiotic regimens include cefotetan or cefoxitin plus doxycycline, with transition to oral therapy once the patient improves clinically.

Pain Management and Complications

Pain management in patients with PID is an essential component of treatment. Analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs), can be used to control acute pain. In patients with chronic pelvic pain, multidisciplinary approaches may be required including pelvic physical therapy, chronic pain management and, in some cases, surgical intervention to relieve pelvic adhesions.

Severe complications of PID, such as tuboovarian abscesses, may require surgical drainage or laparoscopic intervention. Infertility secondary to PID can be managed with assisted reproductive techniques, although success may be limited in cases of extensive tubal damage.

PREVENTION

Prevention of PID is critical to reduce its incidence and long-term complications. Preventive strategies include education on safe sexual practices, screening and early treatment of STIs, and the use of barrier methods.

Education and Screening

Sex education is crucial for the prevention of PID, particularly in adolescents and young women. Educational programs that promote condom use and partner reduction can reduce the risk of STIs and thus PID.

Regular screening for STIs, especially N. gonorrhoeae and C. trachomatis, in high-risk populations is an effective strategy for early detection and treatment of asymptomatic infections that could progress to PID. Current guidelines recommend annual screening for all

sexually active women under 25 years of age and older women with risk factors.

Vaccination

Vaccination against human papillomavirus (HPV) has also been shown to reduce the incidence of infections that predispose to PID, although not directly to N. gonorrhoeae or C. trachomatis infection. HPV vaccination can prevent cervical cancer and other complications that may increase the risk of PID.

Partner Treatment and Spread Reduction

Treatment of sexual partners of women with PID is crucial to prevent reinfection and the spread of STIs. Sexual partners should be simultaneously evaluated and treated for the same infections. Partner notification strategies and empiric treatment can be effective in controlling the spread of STIs in high-risk populations.

CONCLUSION

Pelvic Inflammatory Disease represents a significant challenge to women's reproductive health globally and in Mexico. Understanding the epidemiology, pathophysiology and pathogenesis of PID has advanced, but early diagnosis and appropriate treatment remain crucial to minimize long-term sequelae.

Implementation of advanced diagnostic strategies and effective antibiotic treatments, along with comprehensive preventive approaches, can significantly improve clinical outcomes and reduce complications associated with PID. Continued research is necessary to optimize therapeutic strategies and improve the quality of life for women affected by this debilitating disease.

Conflict of Interest: The authors declare that they have no conflict of interest with the publication of this manuscript.

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